

or  $^3\text{H}$ -uridine. Stimulated synthesis, as measured by incorporation rates of the radiolabeled nucleosides, was noted for SARs less than 50 W/kg, although the effect was not dose dependent. This was interpreted as a generalized effect of RF on cells. When the SAR was increased, the response decreased. For example, at 74.2 W/kg, the mean uptake ratio approached values of the control cells. This was interpreted as an RF effect in a specific phase of the cell cycle. Effects were observed 1, 3, and 5 days postexposure but had a tendency to be reversible. There were no observable effects on cell morphology or viability. The authors conclude that the RF energy modulated DNA and RNA synthesis and had a direct, nonthermal effect on cell proliferation. The mechanism leading to these effects is unknown.

Byus et al. (1988) observed significant increases in ornithine decarboxylase (ODC) activity in three cell lines exposed for 1 hour at 450 MHz, AM at 16 Hz (depth = 75 to 85 percent): Reuber H35 hepatoma cells, Chinese hamster ovary cells (CHO), and 294T human melanoma cells. ODC is an enzyme that is essential for nucleic acid and protein turnover as well as for neoplastic transformation of cells. Increased ODC activity persisted for more than 3 hours after exposure in the H35 and CHO cells but returned to control levels in the 294T cells. ODC activity increased at modulation frequencies of 10, 16, and 20 Hz, but was not significantly affected at 5, 10, 60, and 100 Hz. Exposure produced no effects in controls or TPA-stimulated DNA synthesis.

Litovitz and colleagues (1993) examined the role of coherence time on ODC activity by amplitude-modulated (55, 60, or 65 Hz) microwaves. Coherence time was "defined as the time interval over which one can reasonably predict the frequency, phase, and amplitude of the field." The AM signal was transmitted for times between approximately 0.1 to 50 seconds. No enhancement of ODC activity was observed for exposure to 915-MHz MW, but ODC activity doubled when the carrier was modulated, and the ELF signal "was the critical factor in eliciting cellular response."

### 3.3.9.3 Summary

Two *in vivo* studies provide limited support for the theory that microwave electromagnetic energies may be tumor promoters or co-carcinogens (Szmigielski et al. 1982; Szudziński et al. 1982). The outcome in the study by Szmigielski et al. (1982) must be viewed as that of the three independent experiments and not as replicates. The reliability of the dosimetry in studies by Szmigielski et al. (1982) and Szudziński et al. (1982) is questionable because of the "gang" exposure technique used. Gang exposure may enhance the SAR due to proximity effects.

An independent attempt to replicate the Szmigielski study had key methodologic differences. Santini et al. (1988) concluded that they did not observe an acceleration in cancer development as seen by Szmigielski and colleagues. According to Szmigielski and Gil (1989),

This study [Santini et al. 1988] indicates that neoplastic cells already transformed and passively implanted to new host are not influenced by nonthermal MW fields and further growth of transplantable tumors is not affected by exposure to MWs. The situation here is different from chemical induction of neoplasms or spontaneous tumors, where first induction and promotion of carcinogenesis occur and transformation of cells is followed by growth and spread of neoplasms, partially controlled by the immune system.

In the study (Kunz et al. 1985; Guy et al. 1985) where the collapsed data on primary malignancies demonstrated a significant difference, it is important to note that there were no reliable differences in 155 other end points; i.e., the animals were generally healthy. In a discussion of this point, the researchers state, "The collapsing of sparse data without regard for tissue origin is useful in detecting possible statistical trends, and the finding here of a relative increase in primary malignancies in the exposed animals is provocative; however, when this single finding is considered in the light of other parameters evaluated, it is ques-

tionable if the statistical difference reflects a true biological activity" (Guy et al. 1985).

The *in vitro* studies of Balcer-Kubiczek and Harrison are suggestive of synergistic initiation. Two of the studies demonstrated that MW + the promoter, TPA, increased the transformation rate. If the cells are treated with a known initiator, such as x-rays, then treated with MW and TPA, the transformation rates increase well above those of just MW + TPA or x-rays + TPA. However, because C3H/10T $\frac{1}{2}$  cells are genetically unbalanced, it is possible that their response may not be typical of the response of normal cells under the same exposure protocol. These results have not been replicated in an independent laboratory.

Although *in vitro* studies are important in the elucidation of mechanistic principles, the studies reviewed here are far from conclusive. There are too few studies, they do not evaluate the same end points, and they have not been replicated independently. In fact only one study design, that by Balcer-Kubiczek and Harrison, has been partially replicated by the original researchers. Obviously, much more work is necessary before the significance of these studies can be determined.

## 3.5 HUMAN STUDIES

Reports of potential health effects in humans include epidemiology, clinical investigations,

and accident/incident or case reports. Studies have focused on occupational groups including radar workers, VDT operators, physical therapists, and heat-sealer operators. Individuals involved in one avocation, ham-radio operators, have been evaluated. Cross-sectional surveys have been used a great deal, although a few case-control studies have been used to evaluate general and specific causes of morbidity and mortality. Some clinical investigations contain elements of cross-sectional surveys. For example, both disease and exposure are ascertained simultaneously, but the researchers may not include a control group.

Accident and incident reports involve the investigation of a purported overexposure of a small number of individuals. These reports will be treated separately from the epidemiology and clinical studies. A number of literature reviews that address human studies have been published and are available to the interested reader (Silverman 1973, 1980, 1985; Albrecht and Landau 1978; Michaelson 1983; Hill 1984; Roberts and Michaelson 1985; Heynick 1987; Dennis, Muirhead, and Ennis 1991a, 1991b; WHO 1993). Results of epidemiologic and clinical investigations are in Table 3-15.

### 3.5.1 Epidemiology

Epidemiology is the systematic study of the frequency and distribution of disease in groups of people to try to determine if patterns exist

Table 3-14. Interpretation of Epidemiologic Data

| Rate Ratio      |                 |          |
|-----------------|-----------------|----------|
| (-) Association | (+) Association | Strength |
| 0.9-1.0         | 1.0-1.2         | None     |
| 0.7-0.9         | 1.2-1.5         | Weak     |
| 0.4-0.7         | 1.5-3.0         | Moderate |
| 0.1-0.4         | 3.0-10.0        | Strong   |
| < 0.1           | > 10.0          | Infinite |

After Monson (1990).

Strengths of association: Consistency of observation; specificity of exposure and disease; temporal nature; cause must precede effect; dose-response effect; biologic plausibility; coherence with generally known facts; experimental modification of effect; statistical significance (Hill 1965; Doll 1984; Monson 1990; Susser 1991).

Table 3-15. Epidemiology Studies and Clinical Investigations

| Design                     | Exposure Assessment  | Study and Comparison Groups   | Results   | Reference(s)                          |
|----------------------------|--|---|---|---------------------------------------|
| MORBIDITY AND MORTALITY    |  |   |   |                                       |
| Cohort                     | Estimated exposure using classification scheme; evaluated morbidity and mortality in U.S. Navy personnel   | 20,000 radar workers in high- and low-exposure groups; mostly white males           | No differences in low/high groups for mortality; significant difference within high-exposure group in certain areas for mortality and morbidity | Robinette, Silverman, and Jablon 1980 |
| Cohort                     | Health questionnaire, review of medical records, analysis by MW exposure and years of service in Moscow embassy  | 1719 embassy workers and 1228 dependents, 2460 controls and 2072 control dependents | No effects directly attributable to MW exposure   | Lilienfeld et al. 1978                |
| Non-concurrent prospective | Death certificates, social security information and various other sources; estimates of power density and assignment to groups based on potential exposure | 1477 white, male subjects, controls: U.S. population, and physician specialists     | No reliable findings of MW-induced death; increased rates for Hodgkin's disease and cirrhosis of the liver                                      | Hill 1988                             |
| Cross-sectional            | Evaluation of environmental conditions in radar stations then physical examination   | 322 radar workers and 220 controls  | No significant differences in results of clinical exams   | Djordjevic et al. 1979                |

Table 3-15. (Continued)

| Design                            | Exposure Assessment  | Study and Comparison Groups               | Results   | Reference(s)                       |
|-----------------------------------|--|---|---|------------------------------------|
| Clinical study                    | Radar workers received physical exam and interview; reexamination of 100 subjects                                | 226 MW exposed and 88 controls            | Variable differences in bloodborne end points attributed to interpretation  | Barron, Love, and Baraff 1955      |
| Clinical follow-up study          | Radar workers interviewed by physician; physical exams performed when indicated by history or lab study          | 335 MW exposed and 100 controls           | No remarkable findings  | Barron and Baraff 1958             |
| Clinical                          | Standardized written tests; visual reaction time and WBC phagocytosis  | 1170 exposed and 689 controls             | Significant differences in visual reaction time for male soldiers; reduced memory function for exposure > 10 $\mu\text{W}/\text{cm}^2$ ; WBC phagocytosis affected in some groups | Chiang et al. 1989                 |
| OCULAR EFFECTS: MICROWAVE WORKERS |  |   |   |                                    |
| Clinical study                    | Used an exposure index to estimate MW exposure   | 179 exposed; 70 controls                  | No significant increases in cataracts   | Zaret and Eisenbud 1961            |
| Case control                      | Estimated MW exposure by classifying men as radar workers or nonradar workers; evaluated potential for cataracts | 2946 radar workers; 2164 nonradar workers | No association observed between groups  | Cleary, Pasternack, and Beebe 1965 |
| Clinical study                    | Ophthalmic exam and detailed work history  | 736 MW workers and 559 controls           | Association observed with duration of work with MW, exposure score, and an interaction effect   | Cleary and Pasternack 1966         |

Table 3-15. (Continued)

| Design          | Exposure Assessment   | Study and Comparison Groups                                      | Results   | Reference(s)                         |
|-----------------|---|--|---|--------------------------------------|
| Cross-sectional | Exam with ophthalmoscope and slit lamp  | 200 MW workers, 200 controls                                     | Greater prevalence of lens changes in microwave workers   | Majewski 1968                        |
| Clinical study  | Reported incidence rates and total cases of cataract  | Not reported   | Relatively stable incidence rate  | Odland 1972                          |
| Clinical study  | Ophthalmic examination for opacities, vacuoles, and posterior subcapsular iridescence         | 91 MW workers and 135 controls                                   | Results do not support a causal hypothesis  | Appleton and McCrossan 1972          |
| Clinical study  | Ophthalmic examination per Appleton and McCrossan (1972)                                      | 1542 MW workers and 801 controls                                 | No difference between groups  | Appleton et al. 1975                 |
| Clinical study  | Ophthalmic examination and work history per Appleton and McCrossan (1972)                     | 477 MW workers and 340 controls                                  | No significant differences observed   | Shacklett, Tredici, and Epstein 1975 |
| Clinical study  | Slit-lamp examination for lens translucency assignment of subjects to low or high MW exposure | 507 workers in high group; 334 workers in low group              | No association between MW exposure and lens effects; association observed with lens effects and age | Siekierzynski et al. 1974            |
| Clinical study  | Ophthalmic examination for lens changes   | 121 radar workers; 11 of these had received no known MW exposure | Observed age dependence in MW workers with cataracts  | Castren et al. 1982                  |

Table 3-15. (Continued)

| Design                              | Exposure Assessment  | Study and Comparison Groups                                    | Results   | Reference(s)                         |
|-------------------------------------|--|--|---|--------------------------------------|
| Clinical study                      | Slit-lamp examination with graded scale of lens translucency                 | 3 groups of 1000 each: MW exposed, controls, and juveniles     | Observed correlation of lens translucency with age and power density (MW exposure)      | Zydecki 1974                         |
| Clinical study                      | Slit-lamp examination  | 1000 workers in high exposure group; 180 in low exposure group | No differences between cases and controls   | Sadzikova 1974                       |
| Clinical study                      | Slit-lamp examination for lens opacities; ophthalmoscopic exam of the retina | 68 MW exposed and 30 controls                                  | Observed more retinal lesions in MW exposed group                                       | Aurell and Tengroth 1973             |
| Clinical study                      | Slit-lamp examination  | 53 MW exposed and 39 controls                                  | Observed higher percentage of posterior subcapsular cataracts in exposed group          | Hollows and Douglas 1984             |
| OCULAR EFFECTS: PHYSICAL THERAPISTS |  |  |   |                                      |
| Cohort                              | Mailed questionnaire   | 3093 men   | Bilateral cataracts showed dose-response effect, no differences in unilateral cataracts | Stellman and Stellman 1980           |
| Cohort                              | Mailed questionnaire   | 3004 men   | No significant cataracts for age-adjusted data  | Hamburger, Logue, and Silverman 1983 |
| OCULAR EFFECTS: PLASTICS WELDERS    |  |  |   |                                      |
| Clinical study                      | Interview and eye exam of cornea, lens and fundus                            | 8 plastic welding machine operators                            | Conjunctivitis in 20% of subjects; no reported effects on lens, retina                  | Kolmodin-Hedman et al. 1988          |

Table 3-15. (Continued)

| Design   | Exposure Assessment   | Study and Comparison Groups  | Results  | Reference(s)              |
|--|---|--|--|---------------------------|
| OCULAR EFFECTS: VDT OPERATORS                                |   |  |  |                           |
| Cross-sectional  | Complete eye examination and self-administered questionnaire                              | 379 employees who may use a VDT  | Found no association between VDT use and eye abnormalities                         | Smith et al. 1982         |
| Case-referent  | Ocular history and questionnaire  | 379 VDT workers and 126 referents  | No differences in pathologic lens opacities  | Boos et al. 1985          |
| Cross-sectional  | Ocular examination and medical history  | 29,714 telephone employees; 64/36 male/female ratio                          | Prevalence lower for low-exposure than high-exposure group                         | Bonomi and Bellucci 1989  |
| NERVOUS SYSTEM AND CARDIOVASCULAR EFFECTS: MICROWAVE WORKERS |   |  |  |                           |
| Work place survey and clinical study                         | Review subjective complaints and objective signs  | 162 workers exposed to centimeter waves                                      | Significant increases in certain neurological signs                                | Klimkova-Deutsova 1974    |
| Clinical study   | Evaluation of subjective and objective changes  | 1000 workers in high-exposure group; 180 in low-exposure group; 200 controls | Differences in certain subjective symptoms and in vascular function                | Sadcikova 1974            |
| Clinical study   | Evaluation of functional disorders including neurosis, abnormal ECG, and gastrointestinal | 507 workers in high group; 334 workers in low group                          | No association between MW exposure or duration of exposure and functional disorder | Siekierzynski et al. 1974 |
| Cross sectional  | Evaluation of neurological conditions in radar workers                                    | 322 radar workers and 220 controls   | No significant differences in ECG and neurosis                                     | Djordjevic et al. 1979    |

Table 3-15. (Continued)

| Design  | Exposure Assessment  | Study and Comparison Groups   | Results  | Reference(s)                          |
|---|--|---|--|---------------------------------------|
| Clinical study  | Neurologic, psychometric, and blood analysis; and evaluation of protein bands in CSF | 17 exposed and 12 controls  | No effects on neurological, psychometric, or blood parameters; significant effect on a specific CSF protein band | Nilsson et al. 1989                   |
| NERVOUS SYSTEM AND CARDIOVASCULAR EFFECTS: PHYSICAL THERAPISTS  |  |   |  |                                       |
| Cohort  | Questionnaire  | 3093 men  | Effects observed on blood pressure and blood disorders, but not on heart disease                                 | Stellman and Stellman 1980            |
| Cohort  | Mailed, self-administered questionnaire (58% response rate)                          | 3004 men  | Significant differences in heart disease   | Hamburger, Logue, and Silverman 1983  |
| NERVOUS SYSTEM AND CARDIOVASCULAR EFFECTS: PLASTICS WELDERS     |  |   |  |                                       |
| Cross-sectional   | Interview, 2-point discrimination (2-PD) and EnEG                                    | 113 RF exposed and 23 female controls; subgroup of 38 had neurologic evaluation | Observed more neurasthenia, reduced 2-PD and reduced nerve conduction velocity in RF exposed individuals         | Kolmodin-Hedman et al. 1988           |
| NERVOUS SYSTEM AND CARDIOVASCULAR EFFECTS: TV AND RADIO WORKERS |  |   |  |                                       |
| Clinical study  | Physical examination and blood protein analysis                                      | 51 TV workers, 58 radio workers, 59 controls                                    | Significant differences in blood proteins  | Pazderova, Pickova, and Bryndova 1974 |
| REPRODUCTIVE EFFECTS: MICROWAVE WORKERS                         |  |   |  |                                       |
| Clinical study  | Questionnaire and andrologic and endocrinologic clinical exams                       | 31 MW exposed men and 30 controls   | Significant differences in semen parameters  | Lancranjan et al. 1975                |

Table 3-15. (Continued)

| Design                                    | Exposure Assessment   | Study and Comparison Groups       | Results   | Reference(s)                          |
|---|---|-----------------------------------|---|---------------------------------------|
| Cross-sectional                           | Questionnaire and andrologic and neuroendocrine exams   | 20 MW exposed men and 31 controls | Significant differences in semen parameters   | Weyandt 1992                          |
| Clinical study                            | Interview   | 335 MW exposed and 100 controls   | No difference in reported fertility data  | Barron and Baraff 1958                |
| Case control                              | Personal interview with father and mother; search of hospital records; review of military records and classification as to likelihood of job title to have radar exposure | 216 matched subjects              | Demonstrated an association between history or radar work and mongolism in Baltimore area; no significant differences in follow-up study  | Sigler et al. 1965                    |
|   |   | 344 matched subjects              |   | Cohen et al. 1977                     |
| REPRODUCTIVE EFFECTS: PHYSICAL THERAPISTS |   |                                   |   |                                       |
| Cohort                                    | Records of birth outcomes and occupation identified in computerized registry;   | 2018 women and 2043 offspring     | No differences with general population  | Kallen, Malmquist, and Moritz 1982    |
| Nested case control                       | cases/controls from cohort; self-administered questionnaire (104 respondents)   | 36 cases, 67 controls             | Significant differences in perinatal death and major malformations for (often/daily) users of shortwave diathermy and ultrasound  |                                       |
| Case control nested in a cohort           | Mailed questionnaire to female subjects identified by linkage of registers  | 204 cases and 483 controls        | Significant increase in spontaneous abortion for use of shortwave diathermy $\geq 5$ h/wk, when controlled for confounders, the result was not significant; difference for low-dose group in congenital malformations attributed to recall bias | Taskinen, Kyyronen, and Hemminki 1990 |
|   |   | 46 cases and 187 controls         |   |                                       |

Table 3-15. (Continued)

| Design                              | Exposure Assessment  | Study and Comparison Groups         | Results  | Reference(s)   |
|-------------------------------------|--|-------------------------------------|--|--|
| Case control nested in a cohort     | Telephone interview of female subjects using method tested in Larsen and Skotte (1991)   | 54 cases and 248 controls           | No significant differences by exposure duration or peak level of exposure  | Larsen 1991  |
|                                     |  | 270 cases and 316 controls          | No significant differences in spontaneous abortion, stillbirth, birth weight and prematurity; significant differences in sex ratio | Larsen, Olsen, and Svane 1991  |
| Nested case control                 | Mailed, self-administered questionnaire  | 1753 cases and 1753 controls        | Significant differences in miscarriage for users of MW diathermy   | Stewart and Ouellet-Hellstrom 1991; Ouellet-Hellstrom and Stewart 1993 |
| Cohort                              | Interview by trained nurses using standard questionnaire and review of medical records   | 56,067 women                        | No significant differences   | McDonald et al. 1987, 1988a, 1988b                                     |
| Cohort                              | Mailed, self-administered questionnaire  | 3004 men                            | No significant differences   | Logue et al. 1985  |
| REPRODUCTIVE EFFECTS: VDT OPERATORS |  |                                     |  |  |
| Cohort                              | Reproductive history determined by telephone interview; duration of exposure from company records; measurement data collected at randomly selected work stations | 323 exposed and 407 female controls | No significant differences in spontaneous abortion   | Schnorr et al. 1991  |

Table 3-15. (Continued)

| Design                    | Exposure Assessment   | Study and Comparison Groups   | Results   | Reference(s)                                       |
|---------------------------|---|---|---|--|
| Case control              | Examined pregnancy outcome in women via questionnaire or telephone interview              | 1175 working women  | Association with VDT use > 20 h/wk and spontaneous abortion; no difference in birth defects   | Goldhaber, Polen, and Hiatt 1988                   |
| Case control              | Interview administered in person or by telephone  | 4711 cases with current pregnancies, 19,903 controls; 2164 cases with previous pregnancies, 20,357 controls | Association with VDT use > 15 h/wk and spontaneous abortion in current pregnancies in clerical workers and all occupations; no differences for previous pregnancies | McDonald et al. 1988a                              |
| Case base                 | Random base sample selected from case population; self-administered, mailed questionnaire | 2248 cases and 225 in base sample; 661 cases and 71 in base sample  | No significant differences in spontaneous abortion; no reliably significant differences in congenital malformations   | Nielsen and Brandt 1990<br>Brandt and Nielsen 1990 |
| Case base within a cohort | Linkage of computer data bases followed by a self-administered, mailed questionnaire      | Case and base numbers vary by measured end point  | No significant differences  | Nielsen and Brandt 1992                            |
| Case referent             | Personal interview  | 235 cases and 255 referents   | No significant differences in congenital malformations  | Kurppa et al. 1985                                 |
| Reference cohort          | Personal interview  | 239 office workers who had been pregnant; 60 of these used VDTs; 805 nonoffice work controls                | No differences in threatened abortion, length of gestation, and birth weight  | Nurminen and Kurppa 1988                           |

Table 3-15. (Continued)

| Design                             | Exposure Assessment  | Study and Comparison Groups                                    | Results   | Reference(s)                    |
|------------------------------------|--|--|---|---------------------------------|
| Case control                       | Personal interview   | 334 cases, 333 postnatal controls and 314 prenatal controls    | No association between VDT use and spontaneous abortion   | Bryant and Love 1989            |
| Case control                       | Mailed questionnaires  | Selected from 3 cohorts above                                  | No significant differences in spontaneous abortion after accounting for confounding; significant increases in birth defects | Ericson and Kallen 1986a        |
| Cohort                             | Linkage of birth and occupational registries using personal identification number    | High-, medium-, and low-exposure cohorts from 2 time periods   | No significant differences in malformations, perinatal death, or spontaneous abortion; effects on birth weight (see text)   | Ericson and Kallen 1986b        |
| Case control                       | Telephone interview  | 439 cases for spontaneous abortion study and 909 controls      | No significant differences  | Windham et al. 1990             |
| Cohort                             | Linkage of registry information: estimation of VDT use employer and trade union      | 4117 births  | No significant differences  | Westerholm and Ericson 1986     |
| REPRODUCTIVE EFFECTS OTHER STUDIES |  |  |   |                                 |
| Case control                       | Examination of birth registry for 20 birth defect categories and paternal occupation | 14,415 live births, 2 controls per case                        | No significant differences for occupations with potential RF exposures  | Olshan, Teschke, and Baird 1991 |
| Case control                       | Registry information used to select subjects; mothers interviewed                    | 573 cases with 733 cardiovascular malformations, 1055 controls | No significant differences in usage of VDTs and microwave ovens in case and control mothers                                 | Tikkanen and Heinonen 1991      |

Table 3-15. (Continued)

| Design                     | Exposure Assessment   | Study and Comparison Groups   | Results  | Reference(s)                          |
|----------------------------|---|---|--|---------------------------------------|
| Cohort                     | Comparison of birth and malformation registries for women plastics welders  | 305 women   | No remarkable findings   | Kolmodin-Hedman et al. 1988           |
| CANCER: OCCUPATIONAL       |   |   |  |                                       |
| Cohort                     | Estimated exposure using classification scheme for U.S. Navy occupations  | 20,000 radar workers in high- and low-exposure groups                           | Increased MR for malignant neoplasms of the lymphatic and hematopoietic systems; significant increase in respiratory cancer for high Hazard Number         | Robinette, Silverman, and Jablon 1980 |
| Cohort                     | Death certificates, medical records, and questionnaire  | Moscow and Eastern European foreign service personnel and dependents            | No significant differences in mortality or morbidity   | Lilienfeld et al. 1978                |
| Non-concurrent prospective | Death certificates, social security information, and classification into exposure groups  | 1477 white, male subjects, controls: U.S. population, and physician specialists | No significant increase in mortality for U.S. controls; significant increase in gall bladder and bile duct cancer in comparison with physician specialists | Hill 1988                             |
| Cohort                     | Determined leukemia cases among active navy personnel and compared with U.S. data base and National Cancer Institute Surveillance, Epidemiology, and End Results population | 102 cases, comparison with SEER population                                      | No significant differences for occupations most likely to be exposed to RF   | Garland et al. 1990                   |

Table 3-15. (Continued)

| Design                     | Exposure Assessment  | Study and Comparison Groups   | Results   | Reference(s)                         |
|----------------------------|--|---|---|--------------------------------------|
| Cohort                     | Self-administered questionnaire  | 3004 male physical therapists   | More malignant melanoma than expected   | Hamburger, Logue, and Silverman 1983 |
| Population-based           | Review cause of death in 218 occupational classes  | 438,000 deaths of white males in Washington between 1950 and 1979       | Significantly increased acute leukemia in TV and radio repairmen  | Milham 1982                          |
| Population-based           | Review cause of death in 219 occupational classes  | 486,000 deaths of white males in Washington between 1950 and 1979       | Significant increase in acute leukemia in TV and radio repairmen  | Milham 1985a                         |
| Cohort                     | Evaluation of a cluster of testicular cancer; 5 of 6 cases confirmed by evaluation of pathology slides | 6 male policemen  | Significantly higher number of observed versus expected cases   | Davis and Mostofi 1993               |
| CANCER: GENERAL POPULATION |  |   |   |                                      |
| Population-based           | Review of ARRL magazine obituaries and death information between 1971 and 1983 in 2 states             | 280 Washington and 1411 California males, compared with U.S. population | Excess of leukemia and myeloid leukemias  | Milham 1985b                         |
| Population-based           | Comparison of FCC files and mortality data base for 2 states   | 402 Washington and 2083 California males, compared with U.S. population | Excess of death by acute myeloid leukemia, significantly fewer deaths than expected for all causes, all malignant neoplasms, pancreatic cancer, circulatory and respiratory diseases, and accidents | Milham 1988a                         |

Table 3-15. (Continued)

| Design           | Exposure Assessment   | Study and Comparison Groups                | Results  | Reference(s)                 |
|------------------|---|--|--|------------------------------|
| Population-based | Comparison of mortality data by FCC class                                   | Same as Milham 1988a                       | Increased multiple myeloma/lymphoma in general licensees, and lymphatic and hematopoietic cancers in technicians | Milham 1988c                 |
| Descriptive      | Exam of local hospital records and terrain maps                             | 3004 first diagnosis cases                 | Cancer morbidity associated with location relative to airport when adjusted for local terrain                    | Lester and Moore 1982a       |
| Correlational    | Evaluation of mortality by sex in counties with and without air force bases | 92 case and 92 population control counties | Statistically significant increase in cancer death in counties with bases  | Lester and Moore 1982b; 1985 |
| Correlational    | Same as in Lester and Moore 1982a   | 91 case and 91 population control counties | No significant differences   | Polson and Merritt 1985      |

MR, mortality ratios; VDTs, video display terminals; ARRL, American Radio Relay League; WBC, white blood cells; FCC, Federal Communications Commission; ECG, electrocardiogram; EnEG, electroneurography; CSF, cerebrospinal fluid.

in morbidity and mortality. These studies compare a group of people who have a common exposure or disease/death with a group of people who do not have that exposure or disease/death. To minimize errors, investigators attempt to control for confounding variables and bias and to explain the role of chance.

In analyzing epidemiology results, we will use criteria suggested in a number of published papers (Hill 1965; Hernberg 1981; Doll 1984; Hennekens and Buring 1987; Ahlbom et al. 1990; Monson 1990; Susser 1991). A compilation of these interpretative criteria is included as Table 3-14. As will become more

obvious, it will not be possible to apply the criteria in Table 3-14 to all of the individual studies, because many studies do not report sufficient information to allow a thorough critique.

A brief review of some of the parameters most frequently used when discussing epidemiologic results is in order. These are the association, the strength of the association, the confidence interval, and statistical significance. An individual epidemiology study will demonstrate an association, i.e., a statistical relationship between some physical, chemical, or biologic agent and the disease under study. Measures of association that are used in the following sections include the relative risk (RR), odds ratio (OR), standardized mortality ratios (SMR), and proportionate mortality ratio (PMR). These measures are briefly defined in the glossary. For more extensive definitions, the interested reader should see standard epidemiology texts (Friedman 1974; Lilienfeld 1976; Hennekens and Buring 1987).

The association may be positive, indicating a risk equal to or greater than the unexposed group, or negative, indicating a reduced risk, as shown in Table 3-14. The strength of the association is represented by the magnitude or size of the risk estimate. The greater the strength of association, the more likely that the increase, or decrease, in risk is due to the agent under study and not some other influence such as a confounding variable. The strength of association is a "point estimate" of risk, but the interpretation of the association includes the confidence interval affiliated with the risk estimate. Usually, a 95% confidence interval (CI) is used in epidemiologic investigations. These are reported as lower and upper limits on the point estimate of risk and interpreted as being 95% confident that the true risk estimate lies within these limits. As we will see later, the confidence interval also helps in the interpretation of statistical significance.

Epidemiology studies evaluate a hypothesis that a disease is associated with some agent. This is done by testing the null hypothesis, i.e., there is no difference in the risk of disease between study groups. To determine if there

is an important difference between groups that requires rejecting the null hypothesis, a test of significance is performed. The level of significance or confidence in these tests is called the *P* value. By convention, most epidemiological evaluations use the  $P = 0.05$  level of significance as a guide, meaning that if  $P \leq 0.05$ , "there is no more than a 5-percent, or 1 in 20, probability of observing a result as extreme as that observed due solely to chance" (Hennekens and Buring 1987).

Because epidemiology involves statistical relationships, the role of chance must be examined. This is important because the disease under study may randomly occur in some members of the group under study, and this occurrence may be an unfortunate coincidence that is attributed to chance. The confidence interval is used as an interpretative tool in examining the role of chance because it "represents the range within which the true magnitude of effect lies with a certain degree of assurance" (Hennekens and Buring 1987). If the confidence interval includes the null value (1.0), then, by definition, the risk estimate is not statistically significant and the results may be explained by chance. If the lower limit of the confidence interval is  $> 1.0$ , then the finding is statistically significant, and the likelihood that it is a chance occurrence is minimized.

Ideally, for a result to be most believable, the confidence interval should be narrow. A broad confidence interval indicates that there is imprecision in the risk estimate, often due to a small sample size.

Sometimes, it may be necessary to combine the statistical analysis of a number of studies in order to compare risk or to derive an overall estimate of risk. This is called a meta-analysis. In a review of this technique, Dickersin and Berlin (1992) observe that the purposes of the meta-analysis include literature review, gain in statistical power, and resolving issues with conflicting results.

The results of epidemiology studies are reviewed below (RF) and in Chapter 9 (ELF). The information below begins with a general review (morbidity and mortality), followed by reviews on the basis of the end point evalu-

ated, such as reproductive effects. Important occupational subcategories, e.g., microwave workers, physical therapists, VDT operators, and others as appropriate, are reviewed for each end point discussed. The final section is an examination of studies of members of the general public.

### 3.5.2 Morbidity and Mortality

A retrospective cohort study evaluated U.S. Naval personnel who served during the Korean War period, 1950 to 1954. Actual exposure information was lacking, so study subjects were grouped into either a low or high-microwave-exposure cohort using six job titles, which were assigned by knowledgeable personnel. The low-exposure group,  $<1$  mW/cm<sup>2</sup>, included radioman, radarman, and aviation electrician's mates. The high-exposure group contained electronics technician (ET), fire control technician (FT), and aviation electronics technician (AT). Some members of this group may have received exposures in excess of 10 mW/cm<sup>2</sup>. A Hazard Number, used to estimate potential exposure, was derived utilizing estimates of the time spent in an occupation and the power of the radar equipment at the time of exposure. Within the high-exposure group, AT and FT had a greater percentage of men with Hazard Numbers higher than the ET group. Because of this difference, analysis was performed for the total, for ET, and for FT + AT. Mortality information was gathered from Veterans Administration and navy records, and mortality ratios were determined both for exposure group and Hazard Number (Robinette and Silverman 1977; Robinette, Silverman, and Jablon 1980). The study could detect 50% excess mortality with a probability of 0.90 at  $P = 0.05$  (Silverman 1985).

Both exposure groups had more favorable age-specific death rates than U.S. white males. The high-exposure group had a small but significant (relative risk,  $RR = 1.26$ ,  $P < 0.01$ ) increase in trauma mortality compared with the controls. A review of death certificates indicated that many accidental deaths occurred in airplane accidents after the Korean

War. This was attributed to the fact that occupationally exposed men were more than twice as likely later to become flight officers than were controls. There were no significant differences in death by suicide or homicide (Robinette and Silverman, 1977). Analysis for cause of death by disease showed no significant differences between exposure groups. Mortality ratios were nonsignificantly elevated for death by malignant neoplasms of the lymphatic and hematopoietic systems ( $MR = 1.40$ ) and other diseases ( $MR = 1.46$ ) for the FT + AT group. Analysis by Hazard Number demonstrated no significant differences for malignant neoplasms, with the highest MR for the respiratory tract ( $MR = 2.20$ ), the lymphatic and hematopoietic system ( $MR = 1.64$ ) and all malignant neoplasms ( $MR = 1.44$ ) (Robinette, Silverman, and Jablon 1980).

Evaluation of morbidity showed that the low-exposure group had significantly increased admissions to naval hospitals for mental disease and accidents, poisonings, and violence. Comparison of disability compensation records found a significant increase in the low-exposure group for mental conditions. If the FT + AT subgroup is compared with the ET rates, there were significant differences in five categories: musculoskeletal system, sensory organs, respiratory system, cardiovascular system, and mental disorders. However, none of these categories was significantly different from the low-exposure group (Robinette, Silverman, and Jablon 1980).

As noted, this study used surrogate measures of exposure because exposure and dose information was not available. This led to the concern that

the so-called "high exposure" rosters were made up of a mixture, in unknown proportions, of men whose actual exposures varied from large to negligible. If a large proportion of the men in fact had very small exposures, the consequence would have been to obscure by dilution any differences which might have been found had it been possible to study a large group of men who had received large exposures (Robinette, Silverman, and Jablon 1980).

Furthermore, "it was not possible to determine non-Navy and non-VA hospitalizations, nonhospitalized conditions, reproductive histories, or subsequent employment histories" (Hill 1988). Strengths of this study include the large numbers of subjects in both cohorts, the use of knowledgeable individuals in generation of the Hazard Number, and statistical analysis.

In the early 1950s, it came to the attention of the U.S. government that the American embassy in Moscow was being irradiated by low-intensity MW radiation (Pollack 1975). The reasons for this irradiation are not known, at least publicly, but speculation suggests it could have been a method devised simply to bother U.S. intelligence agents or an attempt at inducing nervous system effects in embassy personnel, although the latter reason has been discounted (Justesen 1975). In the early 1970s it became public knowledge, which had the effect of increasing funding for studies and increasing awareness of the potential health effects associated with MW exposure. One study examined the health status of foreign service employees and their dependents who had served in the American embassy between 1953 and 1976. The control group was selected from foreign service personnel in other Eastern European countries because of geographic, climatic, dietary, and demographic similarities. Exposure assessment included field measurements, a health questionnaire, a review of medical records and death certificates, and an interview.

Radiation was detectable in the exterior rooms of the embassy building, being transmitted through windows and doors of the embassy building, but not through the walls. Irradiation was intermittent, ranging from a few up to 18 h/d. Frequencies detected included 600 MHz up to 9.5 GHz. Between 1953 and May 26, 1975, there was a single radiation source. The average power density in irradiated rooms was around  $1.5 \mu\text{W}/\text{cm}^2$ . The highest measured value within the embassy was  $10.2 \mu\text{W}/\text{cm}^2$ , and the highest average value was  $3 \mu\text{W}/\text{cm}^2$ . Between May 28, 1975, and February 1, 1977, there were two MW sources. The highest reported value was

$24 \mu\text{W}/\text{cm}^2$  (National Telecommunications and Information Administration 1981).

Mortality rates for the Moscow group were much lower than for U.S. white males and not different from the experience of Eastern European foreign service personnel. This was ascribed to the healthy-worker effect, i.e., a comparison bias (Hernberg 1981). There were no differences in mortality for dependents.

In regard to morbidity, there were no differences in sitting pulse rate, visual acuity, WBC count, electrocardiogram, number of psychiatric exams, and general medical history. About twice as many exposed women had a diastolic blood pressure between 85 and 95 mm Hg, compared with controls. However, after their respective tours ended, the percentages were the same. There were some minor differences in hearing impairment, which do not appear to be related to MW exposure. A review of 70 diseases or health conditions found no differences for females, while there were significant increases in venereal disease and sleepwalking for men. There was a significant difference in appendicitis for the comparison group.

When the cohort was evaluated for any MW exposure, the exposed group had more tropical disease, and the unexposed group had more nervous trouble. Exposed women had increases in the present health summary and boils. Analysis for years of service in the Moscow embassy found significant differences for males in arthritis/rheumatism, back pain, the vascular system, skin and the lymphatic system, and abnormal findings in ears. For females, the only significant difference was in vaginal discharge. These conditions showed a trend of increasing morbidity ratios with the length of service. However, these effects may also be associated with aging.

From questionnaire data, the Moscow group reported more eye problems, but these were "correctable refractive errors." Cases, especially men, reported more of the following symptoms after their tour: depression, irritability, difficulty concentrating, and memory loss. These symptoms are subjective and generally nonspecific, but nevertheless are inter-

esting because of similarities to Eastern European and Russian reports of neurasthenia in MW workers. However, the effects were strongest in the personnel who received the lowest potential exposures. Lilienfeld suggests information bias as a plausible explanation: "In view of the possibilities which had been publicized of the increased danger to their health and that of their children, it is not at all surprising that the Moscow group might have had an increase in symptoms such as those reported" (Lilienfeld 1978).

The authors of the foreign service personnel study (Lilienfeld 1978) and others have discussed the limitations of this study (Silverman 1985; Michaelson and Lin 1987). Chief among these is that the study group was relatively young, and there might not have been sufficient time for development of chronic effects. Also, the response rate on the questionnaires was low (52 percent). Although measurement data were available, retrospective exposure assessment was still crude because of difficulties encountered in assigning exposures to individuals and the variability of the exposure fields themselves. This led to creation of an exposed group that included anyone exposed to more than background radiation.

Prior to the start of World War II, the Radiation Laboratory was started at the Massachusetts Institute of Technology. The Rad Lab operated for five years with the objective of developing microwave radar for military applications. Hill (1988) performed a longitudinal study of the mortality experience of the technical and scientific staff who worked at the Rad Lab between October 1940 and January 1946. Due to difficulties in tracing members of the study population and the increased cost that would be incurred, nonstaff members were excluded from the study. According to Hill, this removed technicians from the study pool, and they were likely to have received some of the highest MW exposures. Mortality data were coded for occupation and cause of death.

Three control groups were used: U.S. white males, white male physician specialists, and internal comparisons within the Rad Lab cohort. The group of 29,725 physician special-

ists, including radiologists, internists, otolaryngologists, and ophthalmologists, were already being studied by epidemiologists at the Johns Hopkins University. The pros and cons of using this group as a control were reviewed by Hill and will not be discussed here, except for two points of interest. Radiologists were excluded from the comparison group, and it was assumed that the remaining physicians had little or no exposure to microwaves. Also, there was an age difference at the time of entry of the Rad Lab staff (28 years old) and the physicians (40 years old) into their respective cohorts. To address this potential selection bias, the remaining physician specialists were combined into a single group, and the cohort selected from this group had an age at entry similar to the Rad Lab cohort. Furthermore, Rad Lab members who were younger than 25 years old at entry were also excluded from this aspect of the analysis.

Exposures were estimated, because there was no exposure or dose information available. Numerical methods were used to determine the power density of two radar units typical of those in operation in 1943. These included a 3-GHz air surveillance unit and a 10-GHz AN/APS-10 aircraft radar. Maximum near-field power density estimates were 2 to 5 mW/cm<sup>2</sup>. According to Hill, anecdotal reports suggest that exposures to some Rad Lab members were sufficient for them to perceive warmth from MW irradiation. A job classification scheme was devised as a surrogate for potential exposure. Because there were no job titles other than staff, the various Rad Lab divisions were ranked according to their potential for exposure. Administrative, research, and office-based field service divisions were placed in the low-exposure category ( $n = 381$ ). Divisions that worked with components, e.g., receivers, beacons, and navigation, were placed in the medium potential exposure category ( $n = 382$ ). The high potential exposure category included those working with systems, field-based field personnel, and members of the transmitter component group ( $n = 764$ ). Work histories were reviewed to determine an individual's predominant job while at the Rad Lab, before assignment to an exposure class. The number of subjects in each group was

limited to white males that could be assigned to a group ( $n = 1477$ ).

Mortality data showed that approximately half the deaths were circulatory system diseases and a quarter were due to neoplasms. When compared with U.S. white males, only one standardized mortality ratio (SMR = 1.03, 95% CI = 0.28 to 2.65) was minimally elevated, and that was a nonsignificant increase in death due to mental, psychoneurotic, and personality disorders. There were significantly decreased SMRs for the following causes of death: all causes, infective and parasitic disease, malignant neoplasms, circulatory disease, respiratory disease, genitourinary disease, skin and cellular tissue disease, and all external causes of death (e.g., accidents). This positive mortality experience of the Rad Lab cohort compared with the U.S. population is ascribed to the healthy-worker effect.

Compared with physician specialists, SMRs were significantly increased for death due to digestive disease (SMR = 2.48, 95% CI = 1.3 to 4.0), Hodgkin's disease (SMR = 10.34, 95% CI = 2.13 to 30.23), malignant neoplasms of the gall bladder and bile duct (SMR = 14.29, 95% CI = 1.69 to 50.29), and cirrhosis of the liver (SMR = 3.90, 95% CI = 1.95 to 6.98). A marginally significant increase was seen for all other residual causes (SMR = 1.52, 95% CI = 1.09 to 2.09). Significantly reduced SMRs were observed for death from circulatory disease and external causes. Scrutiny of the width of the 95% CI shows that estimates for Hodgkin's disease, gall bladder and bile duct neoplasms are somewhat imprecise.

When analyzed by exposure group, the age-adjusted mortality rates per 1000 person-years for all causes of death were the following: low-exposure group, 9.07, 95% CI = 7.55 to 10.6; medium-exposure group, 6.76, 95% CI = 4.2 to 8.63; and high-exposure group, 7.44, 95% CI = 6.38 to 8.50. The confidence intervals overlap and the data do not support a dose-response trend. This general result was found for the other causes of death (Hill 1988).

This study reported generally low mortality rates of a well-defined cohort. However, exposures were estimated, and some misclassification of exposure potential may have oc-

curred by use of the division. In hindsight, it would have been useful to have included the nonstaff technician group in the study. There was no control for potential confounders and a number of sources of potential bias, both points well addressed by Hill.

Djordjevic et al. (1979) evaluated the health status of subjects who had worked with radar between 5 and 10 years. Visits were made to radar stations to study working conditions and environmental factors including noise, humidity, temperature, light, and MW power density. Although variable, power density was typically less than 5 mW/cm<sup>2</sup>. They found less than optimum working conditions: "inadequate air temperature, poor lighting, high noise level, the necessity of paying attention to the radar screens, etc." In the clinical study, there were no significant differences in neurologic, ophthalmologic, otologic, internal, hematologic, and biochemical parameters. Radar workers did report experiencing relatively more headaches, fatigue, and irritability than controls, which the authors credited to poor working conditions. The authors comment that "it seems to us that certain authors, in their clinical studies of human responses to microwaves, very often ignore other harmful occupational factors in radar stations and ascribe all the pathological findings in radar workers to the influence of microwave radiation." Limitations of this study include the lack of sufficient information concerning selection of study subjects, no dose estimates, inadequate exposure information, and too few control subjects.

Barron, Love, and Baraff (1955) examined 226 MW-exposed employees and 88 controls who worked around "S" and "X" band radar equipment. Exposure "varied from an occasional incidental contact with the beam to as much as four hours daily close exposure for periods of from three to four years." Controls had no history of industrial radar exposure. Physical examinations included the central nervous system, hematopoietic system, skin, eyes, gastrointestinal system, and urinary tract. Employees were interviewed to determine any subjective symptoms and reproductive history. Notable differences were found only in a number of hematologic parameters. In prepa-

ration for planned reexaminations, measurement data were collected and radar workers categorized into work zones. Zone A had a minimal power density of  $13.1 \text{ mW/cm}^2$ , while Zone B supported levels between  $13.1$  and  $3.9 \text{ mW/cm}^2$ . The levels in Zone C were felt to be sufficiently low that employees who worked there were excluded from the study. Again, notable changes in hematologic values were found, but these were later discounted because they were due to the "interpretation of one laboratory technician" (Barron and Baraff 1958).

A later report by Barron and Baraff (1958) gave results from medical follow-up of a larger group of radar workers (see Table 3-15). The frequencies of possible exposure were 400 to 9000 MHz, with peak powers of up to 1 megawatt. The results of interviews and exams showed no remarkable differences in ocular results, fertility data, sick leave, hematologic end points, and serum proteins. Seventeen percent of the MW-exposed personnel reported experiencing the sensation of heat, 6% reported symptoms associated with the MW hearing phenomenon, while less than 1% reported other sensations "such as sparking between dental fillings or a peculiar metallic taste." No subjects reported unusual experience due to metallic implants, rings, bracelets, or wrist watches (Barron and Baraff 1958). In these reports, insufficient information is provided on the selection of subjects, and the number of controls is too few. Additionally, none of the end points were tested statistically.

An evaluation of a mixed population in China included children, male soldiers, and male college students. Children were exposed to AM radio, while college students were exposed to radar. The exposed group was limited to individuals who had at least 1 year of exposure. The authors conclude that chronic exposure can change some physiologic parameters, as shown in Table 3-15. However, this conclusion is difficult to support in light of the limited data provided. Measurement data were reported, but the measurement locations are not given. The measured values are low, typically less than  $42 \text{ } \mu\text{W/cm}^2$  for microwave exposure and 22 to 23 V/m for AM electric

fields. It is not known what other potential exposures the groups may have received. The numbers of participants in each group is not stated, and more information is necessary on selection methods (Chiang et al. 1989).

Fucic et al. (1992) evaluated micronuclei in blood samples from a group of microwave workers. No exposure information was provided. They conclude that microwave radiation acts in a manner similar to both x-radiation and chemical clastogens (agents that cause structural changes, primarily breaks, in chromosomes). The methodology in this study is lacking in detail, and hence, the results are not convincing. Exposures were quantified in a large range of frequencies, and the reported power densities represent a spectrum of values from no detectable level of microwaves to potential overexposure. Garson and colleagues (1991) studied chromosome damage in radio linemen who had received chronic exposure at Telecom Australia. Exposures were at frequencies between 400 kHz and 20 GHz, while exposure levels were less than or approaching values recommended in the Australian exposure criteria for E and H fields. Also, measurements of induced currents demonstrated that exposures were less than 100 mA in each leg. Controls were members of the clerical staff. No statistically significant differences were found in chromosome damage. As with the study by Fucic, the range of frequencies is broad; however, measurements of induced currents provide data that can be attributed to personal exposures of individuals.

### 3.5.2.1 Conclusions and Summary

Statistically significant increases in morbidity and mortality were observed in groups defined as having both high and low exposure to microwaves. End points elevated for high-exposure groups included trauma mortality (Robinette and Silverman 1977); blood pressure, venereal disease, and sleepwalking (Lilienfeld et al. 1978); and Hodgkin's disease and cirrhosis of the liver (Hill 1988). However, none of these effects can reliably be associated with MW radiation exposure because of limitations in study design. In some cases, mortality experience was more favorable

in study subjects than the general population (Lilienfeld et al. 1978; Hill 1988).

No exposures or doses could be assigned to individuals in any of the studies, requiring estimates of exposure and assignment of subjects to various exposure groups on the basis of job classification. No observations of adverse effects were consistently made among the studies. Some internal consistency and specificity was observed by Hill. This appeared as an increase in the estimates of Hodgkin's disease when members of the Rad Lab cohort were compared to the U.S. population and physician specialists, although only the latter association was statistically significant (Hill 1988). No significant dose-response relationship was observed.

### 3.5.3 Ocular Effects

These studies have primarily examined the potential for minor lens changes in radar workers, physical therapists, plastics welders, and VDT operators. Although not proven, minor lens changes have been suggested as a precursor to cataract formation. As reported in Section 3.3.2, results in experiments with test animals implicate frequencies between 800 MHz and 70 GHz as most likely in producing ocular effects, including effects on the cornea, iris, lens, and retina. Interaction mechanics reveal that penetration depth and SAR are frequency dependent and that microwaves penetrate to shallower depths in tissue than long-wavelength RF (Hagan and Carpenter 1976; Rosenthal et al. 1976; Taflov and Brodwin 1975; Sullivan, Gandhi, and Taflov 1988).

Although the data from animal experiments cannot be extrapolated reliably to man, they can act as a pointer to areas of potentially greater risk to man. Consideration of the frequencies that have been effective in producing cataracts in animals provides some biologic credibility to the premise that radar workers and physical therapists may be potential target occupations for ocular effects. Often, radar workers are exposed above 800 MHz, while physical therapists may use MW diathermy units (2450 MHz). On the other hand, physi-

cal therapists who use shortwave diathermy (27 MHz), plastics welders (around 27 MHz), and VDT users (typically 15 to 300 kHz) would not be expected to be prime target populations on the basis of observations from animal studies.

#### 3.5.3.1 Microwave Workers

The first suggestion of the potential for ocular effects in humans from MW radiation is usually attributed to a report by Daily (1943). In a study of 45 radar workers, he noted that some workers reported "occasional intra-ocular pain" when working very close to experimental radars in the Naval Research Laboratory. Since that time, a number of studies and reports dealing with the potential for human ocular effects have appeared in the scientific literature.

In the investigation of aircraft company personnel reported earlier (Barron, Love, and Baraff 1955), ophthalmologic evaluations found pathologic conditions in 12 exposed persons and 1 control; 11 of the 12 conditions in the exposed group were not attributed to radar exposure. No explanation could be made of a single case of "punctate retinal hemorrhage." Subjective complaints included "aching eyeballs."

Zaret and Eisenbud (1961) found no significant increases in cataracts as determined by an exposure index. Statistically significant increases "in the occurrence posterior polar defects, luminescence, and early opacification of the lens" were found. They suggest "that the frequency of defects may be dependent upon relative severity of exposure to microwaves."

A case-control study examined the potential for cataract formation in veterans from World War II and the Korean War who had been treated for cataracts between 1950 and 1962. Exposure assessment involved determining the occupational specialty, then classifying these as either radar or nonradar workers. The study could detect a doubling of the relative risk with a probability of 0.80 at  $P = 0.05$ . For all radar workers the  $RR = 0.67$ , less than the null value. Analysis by branch of service found an  $RR$  for army and air force

personnel of, respectively, 0.60 and 2.18. Although elevated, the latter RR was not statistically significant due to imprecision associated with a small sample size. No association was observed as a function of age (Cleary, Pasternack, and Beebe 1965). This study is limited by the lack of dose or exposure information for study subjects.

Cleary and Pasternack (1966) collected detailed information on work history and examined the lenses of MW workers and controls using a double-blind technique. Controls were selected from the same locations and work environments as exposed workers, but they were not matched by age. Ocular exams for subclinical and minor changes to the lens provided information for an "eye score."

By using weighting factors derived from parameters known or believed to be important in cataractogenesis, an exposure index called the exposure score was created, since dose or exposure information was not available. The study, however, did not evaluate cataracts as an end point but examined subcataractous and minor lens changes. A regression analysis led to the conclusion that "eye score is more dependent upon the power output of radar equipment than upon the duration of microwave work." Scrutiny of the type of ocular change indicated that the exposed groups had significantly different eye scores in minor defects, relucency, and sutural defects. Effects appeared to be more highly correlated with individuals who worked in research and development than in other types of MW work. An inquiry into the hypothesis that ionizing radiation could have contributed to the lens defects indicated no association. No conclusion could be drawn concerning cataracts from this study, but the authors found that MW exposure may increase the rate of lens aging.

Majewska (1968) examined the potential for lens changes in MW workers between the ages of 18 and 50, who were potentially exposed at frequencies between 0.6 and 10.7 GHz. The group was composed of 192 men and 8 women who had been employed between 0.5 and 12 years. Age-matched controls were used, but no mention is made of their sex. Eighty-four percent of the MW workers

and 74% of controls had lens changes, a difference reported as significant. To examine the effect of duration of exposure, lenticular changes in 102 of the exposed and 100 controls were graded. For each age grouping, the average grade was higher in the exposed group. Although the results are suggestive, there are a number of limitations. These include the lack of information on microwave dosage and subject selection. Also, it was not stated if exams were performed in a blind manner.

Odland (1972) reported the results of medical follow-up of U.S. Air Force personnel between 1959 and 1968. The incidence rate of cataracts stayed within the range of expected random variation but was not tested statistically. There was an increase in the incidence rate with increasing age of the subjects.

In a clinical investigation, Appleton and McCrossan (1972) assessed preliminary results from an examination of army personnel from Ft. Monmouth, New Jersey. This facility was selected because of a high concentration of powerful microwave emitters. Subjects were selected as "could have been exposed" or "almost certainly had not been so exposed" by health physicists (Appleton 1973). Subjects were evaluated for visual acuity and the presence or absence of opacities, vacuoles, or posterior subcapsular iridescence. Evaluations were performed in a blind manner. No statistical analysis of the data was presented, but the authors suggest that there is no difference between the MW-exposed group and the controls (Appleton and McCrossan 1972). In a later treatise, Appleton et al. (1975) reported no differences between MW workers and controls in a clinical survey at five different locations. Individuals included in the study were selected by the head of the local worker health programs. Subjects assigned to the control group reported little or no MW exposure, but they may have been exposed to ultraviolet radiation, xenon-arc emissions, laser radiation, and broadband emissions from welding operations. The exposed group included individuals who worked "directly with microwaves either as test/development personnel or as operators of the equipment." The assignment of preselected individuals as exposed or controls on

this basis could lead to selection bias and misclassification, does not insure independence between the groups, and does not necessarily ensure that there was actually MW exposure.

The results of the studies by Appleton and coworkers were reexamined by Frey (1985) who disputed their conclusions. According to Frey, certain design elements would tend to reduce the likelihood of finding effects associated with MW exposure. He analyzed the data and reported statistically significant differences ( $P > 0.05$ ) in opacities, which he equated with cataracts. However, this appears to be a misapplication of the chi-square test, since the method of selection of study subjects does not insure that the observations are mutually independent (Remington and Schork 1970). Wike and Martin (1985) criticized Frey's appraisal, noting that in the Appleton study, observed opacities were not necessarily cataracts, as Frey had assumed. They reanalyzed the opacity data with a log-linear technique, finding a significant association with age but not with group.

An air force clinical study with a design similar to that used by Appleton found a general trend of increasing opacities, vacuoles, and posterior subcapsular iridescence with age in both the MW-exposed and control groups. Differences between groups were not significant, but the statistical test used in reaching this conclusion is not specified. Eight exposed individuals and four controls had "clinically significant" lens changes. The exposed subjects underwent a more extensive evaluation, with findings that "absolute evidence of cataractogenic history, disease, or therapeutics was revealed in seven of them, thus making any connection between their lens changes and their occupational exposure to microwave radiation subject to considerable doubt" (Shacklett, Tredici, and Epstein 1975).

Polish researchers defined a group of men who had been exposed to pulsed microwaves at average values  $\geq 0.2$  mW/cm<sup>2</sup>, but not exceeding momentary levels of 6 mW/cm<sup>2</sup>. The control group had exposure  $< 0.2$  mW/cm<sup>2</sup>. Ages ranged from 20 to 45 years old (Czerski, Siekierzynski, and Gidynski

1974). The appearance of the lens was graded for translucency subsequent to slit-lamp examination. Statistical analysis was not possible within each grade, so the data for all grades were combined. No significant differences were found, but an age dependence of lens translucency was demonstrated (Siekierzynski et al. 1974; Siekierzynski 1974). A Finnish study also found an age effect in a population of radar workers with lens opacities (Castren et al. 1982). Djordjevic and associates (1979) found no differences in the prevalence of lens opacities in 322 radar workers and 220 controls.

Zydecki (1974) examined lens translucency in men, women, and children. MW-exposed subjects were "highly preselected," received an average exposure of 4 h/d, and had worked with MW for 1 to 15 years. An equal number of age-matched individuals were assigned to the control group, while a third group included 1000 children and juveniles between the ages of 5 and 17 years. The latter group had the highest degree of lens translucency. Zydecki observed an age effect in the children, with small opacities increasing between 10 and 17 years of age. Statistically significant differences in lens translucency were observed between members of the MW group and the other groups, and between low and high MW-exposure groups. The effect appeared to be correlated with power density, not duration of exposure, a conclusion similar to that reached by Cleary and Pasternack (1966). These results are difficult to interpret, however, because the statistical methods used were not specified, nor were the methods of selection of either control group. As noted, the exposed individuals were "highly preselected," which could have introduced bias into the results. Additionally, the findings of the two studies of Polish workers are not consistent, although the MW-exposed individuals had similar exposure magnitudes (Zydecki 1974; Siekierzynski et al. 1974).

Sadcikova (1974) reported the results of clinical investigations of two exposed groups. Members of the first were exposed at levels up to a few milliwatts per square centimeter, while those in the second were exposed at hundreds

of microwatts per square centimeter. Controls were matched on the basis of age, sex, and "character of work processes which did not involve exposure to microwaves." There were no differences in lenticular opacities between exposed individuals and controls. Details on the selection criteria of subjects and controls and on statistical methods were not provided. Also, the size of the control group is less than optimum.

The potential for retinal effects was investigated in an evaluation of exposed individuals who worked either in radar testing and measurement or in experimental laboratories. Study measures included visual acuity, refraction, slit-lamp evaluation, and retinal exam with an ophthalmoscope. The data indicate that more retinal lesions were found in the MW-exposed group than in controls, although the study population was small and the result was not tested statistically (Aurell and Tengroth 1973; Tengroth and Aurell 1974). It has been noted that during ocular examination of MW workers, ophthalmologists found retinal effects but did not attribute them to MW exposure (Baranski and Czerski 1976).

Hollows and Douglas (1984) reported on cataracts in Australian radiolinemen in a letter to the editor of a journal. Exposure parameters included frequencies between 558 kHz and 527 MHz, with power densities between 0.08 mW/cm<sup>2</sup> and 3956 mW/cm<sup>2</sup>. Controls were age-matched individuals who were not radiolinemen. There were no differences between the groups in nuclear sclerosis, but the exposed group had a higher percentage of posterior subcapsular cataracts, which the authors suggest may be work related.

### 3.5.3.2 Physical Therapists

Two studies of male physical therapists have examined ocular effects. One reported dose-related bilateral cataracts but found no difference in unilateral cataracts. This was based upon data from a mailed questionnaire where 70% of the responses were returned (Stellman and Stellman 1980). Typically, in studies of physical therapists, effects are evaluated by work with either shortwave (27 MHz)

or microwave (2450 MHz) diathermy. These frequencies are different in their penetration depth into the body and in their potential to form hot spots. However, in this study RF exposure was defined as use of both MW and shortwave diathermy. The results were reported as an abstract and have not been published with the detail necessary for a thorough review.

The prevalence of cataracts for a cohort of men (58% response rate) was 0.6%. For men over the age of 35, cataracts were significant when a high-exposure group was compared with a low-exposure group but were not significant after adjustment for age (Hamburger, Logue, and Silverman 1983).

### 3.5.3.3 Plastics Welders

Swedish scientists evaluated men and women who had operated plastic welding machines for more than 5 years. The control group for the women consisted of 23 sewing machine operators, but there was no control group for the men. In interviews, 40% of the women and 23% of the men reported irritative eye complaints, and 90 to 100% of the subjects believed these symptoms were work related, with the highest percentage of complaints from tarpaulin welders. Workplace measurements found that 50% of the units evaluated had at least one measurement point in excess of the Swedish exposure limit, 25 mW/cm<sup>2</sup> at 25 to 30 MHz, although it was not noted if the data were corrected for the duty cycle. Eight people were selected for eye examination by an ophthalmologist, who observed conjunctivitis in an unspecified number of subjects. Thirty-eight other subjects underwent a clinical follow-up exam because of reported eye symptoms. After studying ocular photographs from 27 of these subjects, an ophthalmologist concluded that nine subjects also had conjunctivitis. However, it is possible that the observed effects could be due to exposure to pyrolysis products from PVC welding, which the authors report to be hydrochloric acid, aldehydes, phenols, phthalate esters, and alcohols. Twenty percent of the study group had modest conjunctivitis, but

"Whether this is caused by irritative pyrolysis products and/or a thermal effect of the electromagnetic field cannot be answered by our investigation" (Kolmodin-Hedman et al. 1988).

### 3.5.3.4 VDT Operators

NIOSH performed a cross-sectional survey of newspaper employees. The incidence of all opacities, including minor opacities that did not impact visual acuity, was 33.2% for controls and 27.1% for VDT users; 1.4 to 1.5% of both groups had cataracts that did impact visual acuity. The average length of time subjects had used VDTs was 3.8 years, with a 9.2-year maximum, which may "have been inadequate in terms of amount of exposure to resolve such issues as the putative associations of cataracts and VDT usage" (Smith et al. 1982).

Boos et al. (1985) evaluated ophthalmologic factors in a sample of office employees. No statistically significant differences in pathologic lens opacities were found, but if nonpathologic lens changes were included, the results were marginally significant ( $P = 0.05$ ). Three ophthalmologists performed the eye exams. Differences were observed among these physicians, which may be random occurrences or due to differences among the groups they evaluated. The authors conclude that findings do not appear to have any relation to VDT work.

Bonomi and Bellucci (1989) evaluated ocular pathology in VDT users at the Italian telephone company. Members of the group used a VDT > 2 h/d. Controls used VDTs sparingly or not at all. Questionnaire respondents were 42% of the men, and 75% of the women were VDT exposed. Individuals with senile cataracts and aphakic and pseudoaphakic individuals with a history of senile cataract were combined. This group comprised 74 subjects out of 29,714, or 0.24%, and demonstrated a correlation with age in VDT operators. Data were analyzed for dose-response. The prevalence of cataract was lower (0.195%) in the exposed group than in the unexposed or low-exposure group (0.238%). The authors

conclude that the data show a "lack of any connection between video terminal work and onset of cataract."

As noted, cathode-ray-type VDTs may emit at other spectral regions that have been associated with ocular effects. However, a large number of measurement studies have consistently found levels of optical radiation (UV, blue-light, and infrared) (Murray 1984b; Joyner et al. 1984; Marriott and Stuchly 1986; Hitchcock 1991) and RF fields (Murray et al. 1981; EHD 1983; Cox 1984; WHO 1987) associated with VDTs to be very low compared with human exposure criteria. Therefore, one would not expect any individual spectral component to be associated with ocular effects, as seems to be supported from the few studies reviewed earlier.

### 3.5.3.5 Summary and Conclusions

One consistent trend in these studies is the increasing number of ocular defects with age. The primary ocular effect of concern with MW exposure, cataracts, has been shown to increase with age in populations with no known RF exposure (Chatterjee, Milton, and Thyle 1982; Hiller, Sperduto, and Ederer 1986). Most RF studies examined the association with age but did not control for other possible risk factors. For example, cataracts have been associated with race, sex, educational achievement, UV radiation exposure, residence (rural versus urban), diabetes, blood pressure, severe diarrhea, allergy, and hereditary background (Tengroth 1983; Hiller, Sperduto, and Ederer 1986; Chen et al. 1988; Harding, Harding, and Egerton 1989). Some radar workers may also be exposed to x-radiation emitted from MW generating tubes (Milroy and Michaelson 1972a), a point explored in one study (Cleary and Pasternack 1966).

A consistent weakness in these studies is the absence of exposure information. Attempts to overcome this limitation have generally resulted in the use of scoring techniques or job classification to make crude estimates of exposure. Generally, estimates of exposure duration are coincident with length of time in a

job classification. The frequency of the RF source is generally lacking, but it is a reasonable assumption that many radar workers and physical therapists have been exposed at frequencies that have been associated with ocular effects in test animals.

Most studies found no differences between study groups, although statistically significant differences were observed in three reports dealing with MW (Majewska 1968; Cleary and Pasternack 1966; Zydecki 1974). Interestingly, Cleary and Pasternack found a stronger correlation with the power output of the radar units than with length of MW exposure, while Zydecki found the association to be stronger with power density than exposure duration. Strengths of these reports include the use of age-matched groups in two of the studies (Majewska 1968; Zydecki 1974) and exams performed blind in another (Cleary and Pasternack 1966). Zydecki (1974) and Cleary and Pasternack (1966) had relatively large sample sizes, although Cleary and Pasternack (1966) had fewer controls than exposed subjects. None of these reports have dose data, although Zydecki used exposure groups. There are differences in the scoring scales used in these studies. One used a 3-point scale (Cleary and Pasternack 1966), while the other two have 5-point scales that are similar but not identical. The report of Zydecki lacks sufficient detail concerning methodology, as noted, and is not consistent with the results from most other studies, especially that of Siekierzynski et al. (1974).

VDT operators were not exposed to MW radiation (WHO 1987) but to RF fields with much lower frequencies than those found to be effective in producing cataracts in animal studies. The studies reviewed examined the correlation between VDT use and ocular effects, not RF exposure and ocular effects. In these investigations, there were no significant differences between cases and controls in most measures. Nonpathologic changes were higher in VDT-exposed individuals in one study (Boos et al. 1985) but lower in exposed individuals in another (Smith et al. 1982). A dose-response relationship was not found in the study by Bonomi and Belluci (1989). Studies by Smith et al. (1982) and Bonomi and

Belluci (1989) were cross-sectional surveys that used prevalence as a measure of disease frequency. With this type of design the temporal relationship may not be clear, i.e., it is possible that the disease state could precede exposure. Also, it is not clear if the clinical evaluations were performed in a blind fashion.

In conclusion, the data do not support a causal link between RF/MW exposure and cataract formation in humans, but they do suggest that individuals who work with high-powered MW sources (exposure implied) may have a greater risk of minor ocular aberrations. Other end points of interest in test animals, i.e., effects on the corneal endothelium, iris, and retina, have received little or no attention in studies of humans.

### 3.5.4 Nervous System and Cardiovascular Effects

Effects associated with the nervous and the cardiovascular systems have been combined, because this is consistent with the approach taken in many human studies, especially Eastern European clinical studies. These have indicated that some RF/MW-exposed workers (approximately 30 MHz to 300 GHz) report the occurrence of certain nonspecific symptoms associated with the nervous system, with clinical signs extending to the cardiovascular system (Dodge 1969). These signs and symptoms include headache, nervousness, fatigue, irritability, insomnia, loss of appetite, dizziness, emotional instability, depression, memory loss, thyroid enlargement, sweating, tremor of extended fingers, loss of sexual drive, and impotence (Dodge 1969; Silverman 1973, 1985; Sadcikova 1974; Baranski and Czerski 1976). Collectively, these symptoms and signs are combined into three syndromes that have been viewed as stages in a progressive disease called "radiowave illness" or "microwave sickness or disease" (Dodge 1969; Sadcikova 1974; Glaser and Dodge 1982). Typically, the effects associated with the early stages of microwave sickness are reversible if exposure is discontinued (Healer 1969; Sadcikova 1974; Silverman 1980). The early phase of microwave sickness is called the neurasthenic or

asthenic syndrome. This is marked by fatigue, emotional changes, and minor cardiovascular changes (Dodge 1969). The second general clinical syndrome is neurocirculatory asthenia, a vascular dysfunction via neural responses that increases or decreases heart rate and blood pressure, with changes in the electrocardiogram. The third stage is the diencephalic syndrome which involves insomnia, hallucinations, inhibition of sexual function, and a transient loss of consciousness (Dodge 1969; Silverman 1973).

Early reports of microwave sickness were met with skepticism by Western scientists (Dodge 1969; Healer 1969). A few of the reasons for this will be discussed here but only briefly. The signs and symptoms associated with microwave illness were characterized during workplace surveys that lacked appropriate design elements, or adequate documentation of the methods, and relied too heavily on reported subjective complaints. When documented, some of the methods applied by Russian clinicians were unique and unfamiliar to Western scientists. The most frequently reported signs and symptoms were largely nonspecific, i.e., they were not necessarily distinctly connected with the work environment, and they could be as easily associated with life-style or common clinical disorders as with RF exposure. In some cases, symptoms were of such general nature that most workplace stressors, whether exposure to a chemical or physical agent or a stressful job, could be associated with their production. Symptoms were reported at levels less than those viewed as safe in the West, around 10 mW/cm<sup>2</sup>, and often less than 1 mW/cm<sup>2</sup> (Dodge 1969; Marha 1971; Sadcikova 1974; Baranski and Czerski 1976). Fundamentally, Western scientists had taken a different approach in studying health hazards associated with RF. In the United States few results from workplace surveys were available, with a much greater reliance being placed on the outcome of studies with test animals.

Dodge (1969) and Healer (1969) examined the European and Russian reports, reaching a similar conclusion, that the reports had excluded a good deal of information that would make them easier to interpret and, presum-

ably, more believable. Even so, the large number of reports and the consistency of their findings demanded attention. In fairness to Eastern European scientists of the day, reports by U.S. researchers of the same time period show that they generally do not include information necessary to meet the rigorous scientific standards suggested by Dodge earlier.

Baranski and Czerski (1976) reviewed this dilemma in international health science from an Eastern European perspective. They suggested that some differences may have been caused by difficulties in translation of pertinent literature. In regard to field studies, they state that Eastern European scientists "analyze working conditions very carefully, taking such factors as air temperature and humidity, noise, and lighting into account." The major limitation of all human studies is the absence of adequate exposure information and dose estimates. In recognition of the difficulties in collecting accurate, long-term exposure information, Baranski and Czerski submitted that the best available method is to group workers receiving occupational exposure by a reasonable intensity range, as has been done in a number of studies (Czerski, Siekierzynski, and Gidynski 1974; Sadcikova 1974).

In summary, although the Eastern European and Russian reports were numerous and relatively consistent in their findings, they did not include the methods and documentation that are necessary for acceptance in the West. Combine this with a language barrier and the mistrust that accompanied the Cold War era, and you have a dilemma. Microwave illness as a quantifiable clinical disease is not recognized in the West. This may be supportable from the standpoint of peer review of the scientific methodology of early studies, but that does not diminish the need to define target populations and study designs appropriate to test hypotheses dealing with neurologic effects in humans. Although this has not occurred, the controversy over low-level effects and differences in human exposure criteria did lead to a recognition of the need to harmonize international understanding of RF bioeffects. What evolved was a cooperative agreement between U.S. and Eastern European and Russian governments, which fostered an exchange of tech-

nical information and personnel, international workshops, parallel studies, and numerous technical publications. For further information, the interested reader is directed to the following references: Healer 1969; Dodge 1969; Michaelson and Dodge 1971; Silverman 1973; Baranski and Czerski 1976; Dodge and Glaser 1977; McRee 1980; Glaser and Dodge 1982; and Mitchell 1985.

The occupational group that has received the most attention is MW workers. Other groups that have been examined for neurologic effects include physical therapists, plastics welders, and TV and radio workers.

### 3.5.4.1 Microwave Workers

Baranski and Czerski (1976) examined a large number of Soviet reports and critiqued findings of hypotonia and subjective complaints. Reports on hypotonia cover the period 1948 to 1966. The frequency of hypotonia in subjects varied considerably from 14 to 38%. Variability is also seen in subjective complaints, with the most consistent complaints dealing with headache, sleep disturbance, and fatigue disproportionate to effort. They conclude that the significance of the data is difficult to determine because there is insufficient exposure information, because of technologic and equipment changes, and "because of gradual enforcement of safe exposure limits in the years 1959-1966 early Soviet reports cannot be compared with those published later." Polish studies found similar subjective complaints, but the outcomes of examinations for potential neurologic effects were difficult to interpret because of methodologic differences among clinicians. Changes in EEG were found in two groups of workers, those exposed to modest MW levels (hundreds of microwatts per square centimeter to 1 mW/cm<sup>2</sup>) and higher levels (1 to 10 mW/cm<sup>2</sup>). In their experience, Baranski and Czerski found clusters of workers with bradycardia, changed electrocardiograms, peripheral blood changes, and stomach ulcers, which occurred in 0.5 to 2% of otherwise healthy workers. Typically exposures were  $\geq 10$  mW/cm<sup>2</sup> (MW fre-

quencies not specified) for about 1 h/d. These results could not be generalized due to the small number of workers, but "after introduction of rigorous health and exposure surveillance, as well as partial exchange of personnel, no further cases were noted."

Klimkova-Deutschova (1974) selected 352 detailed case histories from observations made of 530 RF-exposed workers and allocated them into eight groups. The exposed group consisted of workers who were exposed to centimeter waves, apparently including 3 to 30 GHz (McRee 1980). Other RF-exposed workers, who were exposed between 0.45 to 800 MHz, were used as controls. In some cases, estimates of E-field exposure levels are provided. Centimeter-wave workers reported significantly more headaches, fatigue, and excitability than other groups. No age dependence of the symptoms was observed. Tests for objective signs of nervous system dysfunction demonstrated significant differences in four of the groups. These groups were the centimeter-wave workers and workers involved in radio transmission, steel manufacture, and metal welding. Slight alterations were noted in EEG recordings and vigilance, leading to a conclusion that the findings support results found in earlier work dealing with neurologic disturbances. High levels of serum proteins and cholesterol were found in a sample of 40 persons. This report provides too little information to allow a meaningful interpretation. The methods of selection of subjects and the number of workers in seven of the eight groups are not specified. If one considers the occupations of the workers, it is very likely that they may have experienced exposures to other potentially hazardous chemical and physical agents, an issue that is not addressed. Although significance is claimed for certain subjective symptoms and objective signs, the type of statistical test is not identified. The control groups were also RF exposed, and it is not stated if there is a control group for the subsample of workers involved in the biochemical studies. As a paper presented at a conference, it appears that the intention was to summarize the important findings without additional detail, which may

explain, to some extent, the lack of information.

Sadcikova (1974) found increases in a number of subjective complaints including tiredness, a feeling of heaviness in the head, sleepiness, irritability, and partial memory loss. Cardiovascular changes included bradycardia and arterial hypertension or hypotension. An analysis of neurasthenic and cardiovascular effects by duration of employment (< 5 years or 5 to 10 years) showed a general trend of increasing effects with longer employment. This study also reports too little methodologic information, including lack of information on assessment of subjective and objective parameters and statistical evaluation.

Polish scientists studied functional disturbances, including neurasthenic syndrome and cardiovascular function (by electrocardiogram), in men 20 to 45 years old. The workers, who were exposed to pulsed microwaves, were assigned to a high-exposure group or a low-exposure group, a design that allowed researchers to study differences between MW-exposed groups, but not between MW-exposed and nonexposed subjects. Unlike the findings of Sadcikova, no differences were found as a function of duration of exposure, and there was no association with exposure level. Approximately 60% of those examined had functional disturbances, and in 30% of these the disturbances were sufficient to warrant exclusion from further MW exposure (Siekierzynski et al. 1974; Czerski, Siekierzynski, and Gidynski 1974). This finding is not surprising in light of methods of subject selection, which raise questions concerning whether the subjects are representative of Polish MW workers. Subjects were "highly preselected," and "the individuals examined were directed for hospitalization because of doubts as to their fitness for further work in MW exposure conditions by industrial physicians." Some subjects had preexisting conditions that were discovered during the evaluation, and some of these subjects "would probably never be allowed to start work in MW irradiated environment." The lack of finding of effects with exposure group does not support conclusions of MW-induced cau-

sation (Czerski, Siekierzynski, and Gidynski 1974; Siekierzynski 1974). Strengths of this study include elucidation of statistical methods, discussion of selection methods, estimates of potential workplace exposures, and a discussion of limitations of the study design (Czerski et al. 1974).

Djordjevic et al. (1979) studied radar workers exposed to pulsed microwaves, a group reporting more headache, fatigue, and irritability than controls, but no differences in sleep disturbance, memory impairment, or inhibition of sexual activity. There were no differences in RBC or WBC count, hemoglobin, peripheral blood cells, neurocirculatory asthenia as indicated by electrocardiograms, or in neurosis. The authors suggest that the high incidence of subjective complaints is attributable to poor environmental conditions in the workplace.

In a study of MW workers at Lockheed, few workers reported headache and fatigue. Physical examinations found a lower percentage of effects associated with the nervous system and circulatory system in MW workers than in controls (Barron, Love, and Baraff 1955; Barron and Baraff 1958). Goldoni (1990) evaluated 14 occupationally exposed workers and 10 controls. The exposure history included levels from 0.01 to 20 mW/cm<sup>2</sup> at frequencies between 1250 and 1350 MHz, 12 h/d, every other day for 2 years. Workers also had potential x-radiation exposure where the dose equivalents were between 7 and 35 Sv/h. The results of hematologic evaluations showed a significant decrease in thrombocytes and significant decreases in leukocytes and erythrocytes in the peripheral blood.

A study of potential CNS effects was undertaken in a small group of Swedish radar mechanics and engineers. Subjects had "probable exposure to moderate or high levels of [pulsed] microwave radiation," while controls were either "unexposed or minimally exposed." The most common frequencies associated with Swedish radar are 1.3, 3, and 10 GHz. A limited field survey indicated that if shielding were removed from energized magnetrons, it would be possible to exceed Swedish exposure criteria (1 mW/cm<sup>2</sup> for 6

minutes). There were no significant differences in neurologic exams, psychometric or psychiatric tests, or blood samples; 25 of 27 subjects allowed lumbar puncture to collect a sample of cerebrospinal fluid (CSF). There were no differences in routine cytologic and chemical analysis of CSF, but blind classification of CSF proteins by isoelectric bands showed a significant difference ( $P = 0.01$ ) in the protein band with an isoelectric point between 4.4 and 4.5. This finding included 9 of 13 exposed workers and 1 of 10 controls. The authors report a similar finding in monkeys exposed to pulsed microwaves (2.45 GHz) but not in monkeys exposed to CW microwaves, concluding, "The nature and clinical significance of these proteins is still unclear" (Nilsson et al. 1989). This study does not report dose information for any of the subjects, nor does it address other environmental factors, associated with radar work, that could be responsible for the effects. There are also difficulties in generalizing the results from such a small sample, which may not be representative of all radar workers. Due to those limitations, and in light of the absence of a dose-response relationship and demonstrated pathologic effects in the other biologic tests, it is not possible to conclude that the observed effect is detrimental to health.

Questionnaire information from the foreign service study of Moscow-based personnel indicated more subjective complaints of neurasthenic-type symptoms for exposed men. Lilienfeld et al. (1978) attributed this to publicity this group had received concerning the possibility of MW-induced disease for them and their families. When the cohort was evaluated for any MW exposure, the unexposed group had significantly more nervous trouble.

#### 3.5.4.2 Physical Therapists

Stellman and Stellman (1980) report dose-related effects on blood pressure and unspecified blood disorders in a cohort of male physical therapists. No effects were found for heart disease. As noted earlier, the researchers combined data on work with shortwave and

MW diathermy instead of examining morbidity by type of diathermy.

Analysis of the health status of male physical therapists was by shortwave or MW diathermy, with respondents assigned to high- or low-exposure groups. High exposure was defined as employment duration  $\geq 14$  years, an average of  $\geq 17$  treatments administered per week, and the interaction of these two variables. For therapists older than 35 years, the prevalence of heart disease in the high-versus low-exposure group was significantly and consistently elevated. Compared with members of the general population with similar sex, age, and race, the prevalence of heart disease in the study group was less. Analysis by age group showed heart disease to be significantly elevated for shortwave diathermy and joint microwave/shortwave diathermy but not for MW diathermy. A review of questionnaire data indicated that there were 35 cases of ischemia and disorders of conduction and rhythm and 23 cases of other types of heart diseases (Hamburger, Logue, and Silverman 1983). It is possible that the low response rate introduced a selection bias into this study.

#### 3.5.4.3 Plastics Welders

In a Swedish study of plastic welding machine operators, interviews were conducted concerning possible neurasthenic symptoms. E- and H-field measurements of three machine types indicated that tarpaulin machines produce whole-body exposures, ready-made clothing machines primarily expose the extremities (hands and heads), while automatic machines generate the lowest exposures. Tasks required for operation of these machines were "mechanical" and "repetitive." Electroneurography (EnEG) was performed on 38 exposed individuals reporting numbness in their hands, and on all controls. Nineteen percent of the exposed and 9% of the controls reported neurasthenic effects. The authors compare this with a 19% level of neurasthenia reported in solvent workers. Around 42% of the RF-exposed people and 52% of the controls reported headaches, while about 60% of

each group reported tiredness. Forty percent of the total exposed group and 53% of the exposed women related having hand numbness (paresthesia), while only 22% of the controls reported this. Use of a 2-point discrimination (2-PD) test showed a significant decrease in response for RF exposure ( $P < 0.05$ ), and a dose-response relationship between numbness and either machine type (greatest with ready-made) or E field ( $P < 0.05$ ). Around 32% of the subjects and 22% of the controls had disturbed sensory conduction velocities as measured by EnEG, an effect that occurs in about 10% of the general Swedish population. Of those receiving RF exposure, 58% had signs of carpal tunnel syndrome, and the remainder had "a more peripheral effect." The authors suggest "it is possible that the finger sensitivity disturbance in the women working with plastic welding machines might be caused by exposure to the electric or magnetic field" (Kolmodin-Hedman et al. 1988). The results of this study cannot be generalized because the number of subjects is small, and the control group is of one sex and much smaller than the exposed group. The statistically significant findings in the 2-PD test were found by comparing men and women with women controls. Also, with this experimental design, it is possible that the effects preceded exposure. It would be of interest to see if there is an association with contact current, since a high percentage of the subjects reported RF burns.

#### 3.5.4.4 TV and Radio Workers

Czechoslovakian researchers performed physical exams and collected blood samples from radio and television workers and controls. Controls were of similar age, but not age-matched. Subjects worked irregular shifts, while controls worked mostly the morning shift. RF frequencies included 0.64 to 1.5 MHz and 3 to 30 MHz for radio and 60 to 300 MHz for TV. Blood samples were collected at the transmitting site, immediately after exposure to electromagnetic fields. Average and individual levels of blood proteins were within normal physiologic limits. Even

so, there were significant differences between exposed and control subjects at the 1 and 5% levels, although not for each measure for all three groups. Differences were found in total blood proteins, albumin-globulin ratio, albumin level,  $\alpha$  globulin, and  $\beta$  globulin. Changes were more pronounced in radio than TV technicians, possibly due to the greater average age of members of these groups and/or to their greater average duration of exposure. Clinical and laboratory exams revealed no pathologic findings in any of the study individuals (Pazderova, Pickova, and Bryndova 1974).

#### 3.5.4.5 Unspecified Occupation

Kalada and colleagues provide a narrative report on the effects of 40 to 200 MHz RF. The workers were identified as "specialists working with generators of ultra-high-frequency energy." The size of the study population is not specified, but ages were less than 40, and the duration of exposure is greater than 5 years. Greater than half of the sample demonstrated CNS effects involving overactivity of sweat glands, red marks on the skin, and an enhanced pilomotoric reflex. There was a correlation between duration of occupational exposure and neurologic disturbances. A number of neurocirculatory effects were also reported (Kalada, Fukalova, and Goncarova 1974).

#### 3.5.4.6 Conclusions and Summary

Based upon findings in test animals, it seems likely that overexposure to RF fields would influence the nervous and cardiovascular systems. However, the results from the reviewed human studies are inconclusive for a number of reasons. Typically, there were small sample sizes, and controls were not age-matched and in one case not matched for sex. No exposures or information about doses were available, although there were attempts at exposure grouping. At least two such studies found apparently minor perturbations of a measured end point(s) that had no observable

pathologic manifestation (Pazderova, Pickova, and Bryndova 1974; Nilsson et al. 1989).

The most frequently reported observation was an increase in subjective symptoms associated with neurasthenia (Klimkova-Deutschova 1974; Sadicikova 1974; Baranski and Czerski 1976; Lilienfeld et al. 1978; Djordjevic et al. 1979; Kolmodin-Hedman et al. 1988). In one study neurasthenic effects showed an age dependence (Sadicikova 1974), but not in another (Klimkova-Deutschova 1974). Recent findings of nervous system effects include CSF protein band changes (Nilsson et al. 1988) and reduced conduction velocities (Kolmodin-Hedman et al. 1988). These effects need independent verification to show a reliable correlation with RF exposure.

Cardiovascular effects include an increase in heart disease in male physical therapists (Hamburger, Logue, and Silverman 1983). Changes in blood proteins were found in at least two studies (Pazderova, Pickova, and Bryndova 1974), although the type of protein is unspecified in one of these (Klimkova-Deutschova 1974).

### 3.5.5 Effects on Reproduction, Development, and Growth

Two major occupational groups have received the most scrutiny in this area, physical therapists and VDT operators. Reproductive measures in microwave workers have also been examined.

#### 3.5.5.1 Microwave Workers

Romanian researchers reported the outcome of a clinical study of male workers. Their average age was 33 years, and the average time worked with MW sources was 8 years. Exposures were between 3.6 and 10 GHz, at power densities estimated to be tens to hundreds of microwatts per square centimeter. Twenty-two men reported decreased sexual drive and disturbances with erection, orgasm, and/or ejaculation. This was attributed to neurasthenic disturbances, which

reportedly occurred in 25 of the men. Laboratory analysis found significant decreases in the number of sperm per ejaculation ( $P < 0.02$ ), number of motile sperm per ejaculation ( $P < 0.001$ ), and the number of normal sperm per ejaculation ( $P < 0.001$ ), compared with controls. The average level of 17-ketosteroid in the urine was similar in subjects and controls, although normal values were found in only 19 of the subjects. When some of the technicians were reevaluated after removal from MW exposure, about 67% showed an improvement in spermatogenesis. This was interpreted as "an argument for the part played by microwaves in the induction of these alterations" (Lancranjan et al. 1975). In context of the information provided, this conclusion seems premature. Although study measures were significantly affected, the effects have not been reliably correlated with MW exposure. It is possible that other environmental agents associated with MW work could be involved, a factor not considered in the design or analysis. This could also explain the experimental finding when preventative action produced a positive effect on study measures. No details were given concerning subject selection, especially controls. Apparently the selected cases were "volunteers," which may have introduced a bias into the data. These results need independent verification.

In a study of the potential for reproductive effects associated with lead exposure in artillerymen, Weyandt (1992) observed that the control group had a high frequency of reduced sperm count. The control group members were "non-lead exposed" but came from a population that reported a high frequency of microwave work. It was decided to expand the study to evaluate reproductive effects for lead exposure and microwave exposure, which necessitated the selection of a new control group during the study. A finding similar to that by Lancranjan and colleagues was a statistically significant decrease in the sperm count measures in the MW-exposed group. However, no differences were found in sperm morphology, motility, viability, and neuroendocrine parameters. This study is limited by the small number of people involved

and the lack of exposure data, which makes interpretation difficult.

Although not an occupational exposure, microwave radiation (915 and 2450 MHz) is being evaluated in China as a male contraception. This requires heating of the testes to a temperature (40 to 42°C) sufficient to induce sterility. In several hundred volunteers who received treatment from 9 months up to 5 years, there were no changes in sexual function and no observed side effects. Critical questions dealing with genetic effects must be answered before large-scale use of this technique is permitted (Chiang 1988). An evaluation of a small sample of subjects who had received >100 treatments at 20 to 30 W found the MW-induced sterility to be reversible. Histology did find that most testes had damaged tubules (Liu et al. 1991).

Aircraft radar workers reported their fertility history in a medical surveillance program. None of the MW group reported male sterility. More controls reported having no children, where the cause of this was unknown, than for MW-exposed fathers (Barron and Baraff 1958).

In a study designed to examine the association between parental exposure to ionizing radiation and Down's syndrome, an observation was made that fathers of mongols reported a different history of radar exposure than controls. The association could not be viewed as reliable because it was marginally significant ( $P \approx 0.02$ ) and the sample size was small (Sigler et al. 1965; Cohen and Lilienfeld 1970). In a follow-up study, the sample size was enlarged, and the military history of the fathers of both groups was reviewed to provide information on possible radar exposure. Job titles were identified in a blind manner by the National Academy of Sciences Follow-Up Agency (NAS), and military consultants classified them in regard to the likelihood of being exposed to radar. Cohen and colleagues report that it was difficult to ascertain potential radar exposure from information and interviews. In contrast to the original study, for current pairs the control fathers had more radar exposure than case fathers. A reevaluation of the original pairs with the new data showed that a

history of radar exposure was still greater in case fathers, but this was no longer statistically significant. When the current and original categories were combined for interviewed fathers who were definitely exposed or received some exposure, 19.9% of the case fathers and 17.8% of the control fathers had radar exposure. When combined groups were analyzed by information generated by the NAS, 9.8% of the case fathers versus 9.6% of the control fathers had radar exposure. When combined groups were analyzed by both interview and NAS information, radar exposure was found in 22.7% of the case fathers and 20.6% of the control fathers. None of these results represents a significant association between Down's syndrome and radar exposure (Cohen et al. 1977). In this study it is possible that the methods of exposure assessment could have masked an existing effect. However, the results in the expanded study reduced the possibility of the effect being due to chance and supports the hypothesis of no effect.

#### 3.5.5.2 Physical Therapists

A cohort of female, registered physical therapists in Sweden was studied to determine potential reproductive effects of chemicals, x-radiation, and nonionizing radiation. Pregnancy outcome was determined from information in a birth registry, and the outcomes compared with Swedish records of physical therapists. Overall, a favorable outcome was demonstrated with fewer occurrences of stillbirths, perinatal deaths, and major malformations than in the general population, and no significant differences in sex ratio. To further explore occupational parameters of the cohort, a nested case-control study was performed. Cases included women with infants who had died without a major malformation and all infants with major malformations. Controls with a normal birth experience were selected for each case. Controls were matched for age, parity, and delivery time during the year. Ninety-six of 104 questionnaire respondents had worked as therapists during pregnancy, and 33% of the cases and 14% of the controls had used shortwave diathermy often or daily

(OR = 2.03;  $P = 0.03$ , one-sided test). Forty-two percent of the cases versus 27% of the controls had used ultrasound often or daily ( $P = 0.10$ ). Exposures to shortwave diathermy and ultrasound were highly associated, with 14 women reporting use of both types of equipment versus an expected number of 6.5 ( $P < 0.001$ ). No differences were seen in users of MW diathermy (Kallen, Malmquist, and Moritz 1982). The interpretation of the data that the difference is due to random variation cannot be dismissed. This is because of the small sample size in the case-control study and the lack of a robust effect, as indicated by marginal statistical significance.

A Finnish group examined spontaneous abortion and congenital malformations. For spontaneous abortion, odds ratios were non-significantly elevated for 1 to 4 h/wk (OR = 1.2, 95% CI = 0.7 to 1.9) and  $\geq 5$  h/wk (OR = 1.6, 95% CI = 0.9 to 2.7) of shortwave diathermy, and for MW diathermy (OR = 1.8, 95% CI = 0.8 to 4.1). There was a significant difference (OR = 2.5,  $P < 0.01$ ) in spontaneous abortion where shortwave diathermy use was  $\geq 5$  h/wk, and the length of pregnancy was  $> 10$  weeks. When adjusted for the influence of potential confounders, this result was not significant. OR were significantly elevated for ultrasound use  $\geq 20$  h/wk, electric therapy  $\geq 5$  h/wk, and heavy lifting. Congenital malformations were significantly different when shortwave diathermy was used between 1 and 4 h/wk (OR = 2.7, 95% CI = 1.2 to 6.1), but not when used for  $\geq 5$  h/wk (OR = 1.0, 95% CI = 0.3 to 3.1). This finding may be due to recall bias with "the cases reporting slight exposures more than controls." When adjusted for potential confounding by multivariate analysis, shortwave use  $> 1$  h/wk was still significantly increased (OR = 2.3, 95% CI = 1.1 to 5.2). Fewer cases of congenital malformation were observed for the use of MW diathermy (OR = 0.5, 95% CI = 0.1 to 3.9). The authors considered the possibility of differential recall of the respondents since the study examined an 11-year retrospective period, concluding that there appeared to be no major biases. "However, some of the significant associations may be due to chance, since

multiple comparisons were made" (Taskinen, Kyyronen, and Hemminki 1990). Also, the size of the study population for congenital malformations was small.

Concern about a cluster of four infants with malformations out of 25 pregnancies in a physical therapy staff initiated a Danish study, in which 2334 pregnancies were identified in a group of 4021 female physical therapists by comparison of a union registry with birth registries. From this cohort, congenital malformations were examined in a case-referent study. Exposure assessment focused on the first month of pregnancy and included an estimate of exposure time and the type of diathermy electrode. It was felt that this method of exposure assessment was satisfactory, as determined in a pilot study. In that study, measurements were compared with interview data showing that a reasonable estimate of operator exposure could be made from specific interview data. (Larsen and Skotte 1991). Confounders included tobacco use, alcohol use, diseases during pregnancy, and ultrasound and the use of legal drugs during the first month. There were no statistically significant odds ratios by sex of offspring for the duration of exposure (time index) or the level of peak exposure (peak index). Heart malformations were increased for high exposure by both time index (OR = 2.8, 95% CI = 0.4 to 13.7) and peak index (OR = 2.1, 95% CI = 0.5 to 8.0) (Larsen 1991). However, the 95% confidence intervals include the null value indicating that the outcome is nonsignificant and could be due to chance. The width of the confidence interval also indicates a good deal of variability in the estimates due to small sample size. It is possible that knowledge on the part of the participants of the study hypothesis could have biased the results away from the null value. Conversely, nondifferential exposure misclassification could have biased the risk estimates toward the null value.

In a further examination of this cohort, no differences were found in spontaneous abortion, stillbirth/death within 1 year, prematurity, and low birthweight. There were significant differences in the sex ratio, i.e., fewer boys were born to mothers who had indicators

of higher exposure. Analysis of gender distribution by a time-weighted exposure index produced odds ratios of 3.2 (95% CI = 1.5 to 7.1) and 4.9 (95% CI = 1.6 to 17.9) for, respectively, low and high exposure. Significant differences in gender distribution were seen for women receiving both direct and indirect (bystanders) exposure (OR = 3.4, 95% CI = 1.4 to 8.7) and spending more than 20 h/wk in a shortwave diathermy room (OR = 7.0, 95% CI = 2.1 to 31.3). Marginal significance was observed for indirect exposure and work between 11 and 20 h/wk and for low birthweight for boys (OR = 5.9, 95% CI = 1.0 to 28.2). A significant difference in sex ratio was also found for women using plate electrodes (OR = 2.8, 95% CI = 1.5 to 5.5) but not diodes or circuplodes. Accordingly, it has been reported that fields around plate electrodes were the strongest of these three types of electrodes (Larsen and Skotte 1991). The OR increased with higher exposure categories, indicating a dose-related effect. An evaluation of confounders did not affect the outcome (Larsen, Olsen, and Svane 1991). The breadth of the confidence intervals for some of the estimates is relatively large, indicating some imprecision in the estimates because of small sample sizes. The effect on the sex ratio of the offspring must be viewed as hypothesis generating and needs independent verification.

An assessment of early fetal loss was made of members of the American Physical Therapy Association. The study was restricted to women who used microwave or short-wave diathermy 6 months prior to conception or during the first trimester. Questionnaire information (45.1 percent response rate) indicated a significant increase in early fetal loss for women using microwave diathermy (OR = 1.28, 95% CI = 1.03 to 1.59), but not for shortwave diathermy (OR = 1.07, 95% CI = 0.92 to 1.24). When the OR for microwave diathermy was adjusted for prior fetal loss, the result was marginally significant (OR = 1.26, 95% CI = 1.00 to 1.59). Although this point estimate of risk was of marginal statistical significance, the OR increased with reported increases in monthly usage of MW diathermy,

and this exposure-response effect was statistically significant. The opposite was observed for shortwave diathermy, where the OR decreased with increased use (Stewart and Ouellet-Hellstrom 1991; Ouellet-Hellstrom and Stewart 1993).

McDonald and colleagues studied birth outcome in 60 occupations, including physical therapists. End points included spontaneous abortion, stillbirth without defect, congenital defects, low birth weight, and prematurity. Women were interviewed concerning occupation, personal habits, and social factors. In a preliminary analysis of spontaneous abortion, observed to expected ratios (O/E) for physical therapists were 1.04 for current pregnancies and 0.90 for previous pregnancies (McDonald et al. 1986). In the final reports, there were 174 recorded pregnancies for physical therapists. There were no statistically significant differences in any of the outcomes, although the O/E ratio for stillbirth without defect was greater than unity (O/E = 1.15) (McDonald et al. 1987, 1988a, 1988b). This study was designed to examine the effect of occupation, not the effect of specific agents. In that context, it appears that female physical therapists were not an occupational group at increased risk for the adverse reproductive outcomes evaluated.

A prospective study examined spontaneous abortion, perinatal death, birthweight, and congenital malformations in 3096 Swedish women. Physical therapists were included as an occupational category that also included nurses and laboratory workers. The point estimate for spontaneous abortion was slightly, but nonsignificantly, elevated (RR = 1.12, 95% CI = 0.69 to 1.84), while the RR for adverse reproductive outcome was slightly lower than unity (Ahlborg et al. 1989). In this study, some of the occupational categories were broad and may not have had common risk factors, as seems to be the case for the category including physical therapists. This may have increased the numbers for analysis in the category but also may have had a diluting or masking effect.

Logue et al. (1985) examined congenital anomalies in male physical therapists in the

United States The study design is outlined previously (Hamburger, Logue, and Silverman 1983). No significant differences were found for 17 types of anomalies. The authors suggest that the total number of anomalies for first births may be higher than expected when compared with other rates reported in the scientific literature.

### 3.5.5.3 Video Display Terminal Operators

A summary of published epidemiological studies of video display terminal (VDT) users is included in Table 3-15. Some unpublished studies are reviewed by Mackay (1987) and the World Health Organization (WHO 1987). Studies have primarily examined the associations between VDT use and spontaneous abortion and congenital malformation. To date, three studies have found a statistically significant association between VDT use and study measures (McDonald et al. 1988c; Goldhaber, Polen, and Hiatt 1988; Brandt and Nielsen 1990). However, it should be noted that these studies, and most others reviewed later, did not report actual RF exposures or doses for any operators, but instead used "VDT use" in exposure assessment. By so doing, the studies are evaluating the effects of the VDT work station and the work environment on reproductive outcome, and not specifically the effects associated with electromagnetic energies. Only NIOSH has evaluated potential associations using actual RF measurement data reflective of operator exposure. (Another recent study, which reported an increased risk of spontaneous abortion [Lindholm et al. 1992], performed measurements of just ELF magnetic fields, not RF electric and magnetic fields.)

NIOSH researchers studied reproductive outcomes in two groups of communications operators. The exposed cohort consisted of directory-assistance operators who used CRT-VDTs at work. The control cohort was general telephone operators who used work stations that had nothing in common with CRT-VDTs (Petersen 1991). These were either neon-glow tube or LED displays. The

operators were not age matched but were similar in average age, race, education, average lifetime number of pregnancies, and average years employed by a company included in the study. Interview information on lifetime reproductive history was compared with company personnel records to ascertain if the subjects had used a VDT during pregnancy. Payroll records were used to determine actual work hours with a VDT. Extensive measurement data were collected around 48 VDTs, by randomly selecting six terminals in eight Bell South offices (Petersen 1991). Geometric means of measurement data for VDT VLF fields (3 to 30 kHz) were significantly different ( $P < 0.05$ ) from fields associated with non-VDT displays, which were below background levels. Average field strengths at VDT operators were  $< 1.5$  V/m and  $< 0.42$  A/m (Tell 1990). Abdominal exposure to VDT operators was significantly higher than in non-VDT workers. No significant differences were found between the exposed and control groups for live births, stillbirths, and spontaneous abortion during the first trimester of pregnancy (OR = 0.93, 95% CI = 0.63 to 1.38). No dose-response effect was observed when data were analyzed by hours of VDT use per week. Spontaneous abortion was associated with a history of spontaneous abortion, alcohol consumption, cigarette smoking, and evidence of a thyroid disorder (Schnorr et al. 1991).

Workers at Kaiser-Permanente identified a large cohort of women who had pregnancies during a large-scale pesticide (malathion) application in the state of California. From this group, women were selected who had first-trimester miscarriages, reportable birth defects, and normal live births. Information on life-style and VDT use were collected with a finding that the use of VDTs for more than 20 h/wk during the first trimester was associated with an increased incidence of spontaneous abortion (OR = 1.8, 95% CI = 1.2 to 2.8). Birth defects were not significantly elevated for VDT use  $> 20$  h/wk. For women who use VDTs  $< 20$  h/wk or for the category of any VDT exposure versus no VDT exposure, the risk of spontaneous abortion and

birth defects was not statistically significant (Goldhaber, Polen, and Hiatt 1988; Goldhaber 1990). The researchers emphasized that more research is needed to define potential risk factors, which may include job-induced stress, ergonomic considerations, or electromagnetic radiation.

McDonald et al. (1988c) found a modestly significant increase in spontaneous abortion in current pregnancies for Canadian clerical workers (RR = 1.26, 90% CI = 1.10 to 1.44) and all occupational sectors (RR = 1.23, 90% CI = 1.09 to 1.38) who worked with a VDT more than 15 h/wk. No differences were seen in the same sectors for previous pregnancies. A slight increase in risk of spontaneous abortion was observed for all working women who used VDTs in current pregnancies (RR = 1.19, 90% CI = 1.09 to 1.30), but not in previous pregnancies (RR = 0.97, 90% CI = 0.89 to 1.05). The authors attributed the outcome in current pregnancies to recall bias among the study population, because "the grouped analysis suggested that occupations with high VDU use did not have high risks for abortion; the RR for VDU use estimated by this method was 1.06, although with a wide confidence interval (0.8-1.4)." A significant increase in renal urinary congenital defects was observed in current pregnancies (RR = 1.84, 90% CI = 1.07 to 3.15), but not in previous pregnancies (RR = 1.66, 90% CI = 0.81 to 3.25). In discussion of this point, the authors state, "Although a causal relation cannot be dismissed, the nature of the abnormality and the absence of any obvious mechanism or prior evidence suggests that this may be a chance finding." No statistically significant risks were found for stillbirth, preterm birth, and low birth weight.

Nielsen and Brandt (1990) evaluated the potential for medically verified spontaneous abortion and congenital malformation (Brandt and Nielsen 1990) in Danish women. Adjusted risk indicators for both measures were not statistically significant for any work with VDTs, regardless of weekly average time of use. Analysis by type of malformation showed a significant point estimate (OR = 12.0) for hydrocephalus, but the confidence interval was extremely broad (95% CI = 1.38 to 104), indi-

cating much imprecision in the estimate because of the small sample size. No malformation type, other than hydrocephalus, was significantly elevated. For urinary system (OR = 1.29, 95% CI = 0.48 to 3.43) and heart (OR = 0.94, 95% CI = 0.50 to 1.74) malformations, the data were compatible with the null value, i.e., no association between exposure and disease. In a study that linked a trade union file with public health records, Nielsen and Brandt (1992) found no differences between cases (VDT use) and controls for low birthweight, light weight for delivery date, preterm birth, stillborn, perinatal death, and infant death.

Kurppa and colleagues (1985) found a slight negative association in the point estimate of congenital malformations (crude OR = 0.9, 95% CI = 0.6 to 1.2) for women who used VDTs during the first trimester. Cardiovascular defects were modestly increased, but not significant (OR = 1.6, 95% CI = 0.7 to 3.9). Nurminen and Kurppa (1988) saw no unfavorable effects on length of gestation and birth weight by gestational age. Bryant and Love (1989) observed no notable association between VDT exposure and spontaneous abortion when cases were compared with either prenatal controls (OR = 0.81, 95% CI = 0.59 to 1.11) or postnatal controls (OR = 1.14, 95% CI = 0.83 to 1.56). Ericson and Kallen (1986a) did find a significant association in the crude OR for birth defects and some measures. However, after controlling for confounding (smoking and stress) in the analysis, the results for VDT work and all reproductive effects were not significantly different from controls.

Swedish researchers found no effect on hospitalized spontaneous abortion and VDT work for a 1976 to 1977 cohort and a 1980 to 1981 cohort. Birth weight was significantly reduced in the 1980 to 1981 medium VDT exposure group with babies weighing  $< 1500$  g (O/E = 2.2, 95% CI = 1.1 to 4.4), but not in the 1976 to 1977 medium exposure group. Conversely, low birth weight was found in the 1976 to 1977 medium exposure group for babies  $< 2500$  g (O/E = 1.5, 95% CI = 1.2 to 1.8), but not for the 1980 to 1981 medium

exposure group. In the high exposure group, low birth weight in babies <2500 g was marginally significant in the 1976 to 1977 group (O/E = 1.2, 95% CI = 1.0 to 1.4), but not in any of the other three high exposure groups (1976 to 1977 <1500 g, 1980 to 1981 <1500 g, and 1980 to 1981 <2500 g) (Ericson and Kallen 1986b). It is difficult to conclude that birth weight was reliably affected because of the lack of trend and the marginal significance of the results.

Parazzini and colleagues (1993) performed a meta-analysis examining the outcome of nine published studies on reproductive outcomes among VDT operators. Eight of the studies evaluated VDT use, and one examined exposure to RF electric and magnetic fields. The analysis demonstrated no statistically significant effects found for spontaneous abortion, low birth weight, or congenital malformations.

#### 3.5.5.4 Clusters

Clusters are occurrences of a disease or adverse condition that exhibit a temporal or spatial relationship. Evaluation of clustering phenomena has been an important element in the determination of the etiology of a number of occupational diseases (Fleming, Ducatman, and Shalat 1991). Concerns about clusters of adverse reproductive outcomes have been raised after reports of such effects among VDT operators and physical therapists.

In Denmark, concerns were voiced about clustering when there were four instances of congenital malformation in 25 pregnancies among a group of physical therapists. This spawned an epidemiologic investigation (reviewed earlier) that found no statistically significant differences in congenital malformations in the population under study (Larsen 1991). Clustering has also been evaluated in VDT user populations. Reviews have indicated that a causal link with VDT use has not been established (AMA 1987) and that clusters can be explained by chance (Bergqvist 1984; Mackay 1987). As noted by Scialli (1990), clustering "must occur in random events." To

convince yourself of this fact, simply toss an unbiased coin a large number of times, and you will find a number of "heads" clusters and "tails" clusters in this random process.

Models that illustrate the nature of expected clusters have been developed. Based upon results from a sensitive pregnancy test, about 20% of all pregnancies result in spontaneous abortion. Using this number in a user population of 50 million individuals, if 1% are pregnant, this will result in 100,000 spontaneous abortions (Scialli 1990). Blackwell and Chang (1988) suggest that chance could explain 29 clusters per year in a hypothetical population of VDT users in which there is a naturally occurring 15% pregnancy failure rate. Butler (1986) has estimated that "tens or hundreds of 'high' s.a. [spontaneous abortion] incidence rate clusters could randomly appear each year." Bergqvist (1984) suggests that the six clusters of spontaneous abortion and three clusters of congenital malformations that were reported in the United States and Canada in 1979 to 1980 agree with expected numbers. Schnorr (1990) reports that NIOSH has investigated three clusters of miscarriage among VDT operators. An excess of miscarriages was found in one study where "VDTs were not present in the area with the excess." No excess was found in the second study, while the excess could be explained by chance in the third.

#### 3.5.5.5 Other Studies

Paternal occupation and congenital anomalies were evaluated using a population-based registry of liveborn children in British Columbia, Canada. Two controls were selected for each case and matched by hospital, month, and year of birth. Occupational history was determined from information entered on the birth record. The study covered the time period of 1952 to 1973. Occupations were examined by a panel that assigned most likely exposures to 58 categories. Three of these categories have the potential for exposure to electromagnetic radiation including, but possibly not limited to, RF fields: elec-

tronic equipment operators (including radio and TV technicians); electricians, electrical, and electronics workers; and aircraft operators. No significant OR were found for these occupations for the 20 birth defects categories studied. In some cases, point estimates of risk were elevated, but the confidence intervals included the null value. The numbers for aircraft operators were too small for a meaningful analysis of a number of birth defects (Olshan, Teschke, and Baird 1991).

Tikkanen and Heinonen (1991) examined maternal exposures to chemical and physical agents during the first trimester and congenital cardiovascular malformations. Cardiovascular malformations verified by pediatric cardiologists between 1982 and 1984 were included in the study. Mothers were interviewed by midwives using a standard questionnaire that addressed potential exposures at work and at home, including microwave ovens and VDTs. There were no significant differences in the numbers of control and case mothers reporting use of a MW oven or a VDT during the first trimester of pregnancy.

In the study of plastics welders discussed earlier, Kolmodin-Hedman and colleagues (1988) report on a study of malformations for 235 women working with all types of machines and 70 women who had previous exposure in a 10-year period, 1974 to 1984. The comparison group was the Swedish average from registry information. No significant findings were reported, although the detail on the reproductive study is meager.

#### 3.5.5.6 Conclusions and Summary

Studies of RF-induced reproductive effects are necessary because these end points are biologically plausible and coherent with the known facts derived from the outcome of numerous animal studies. The primary occupational groups that have been studied are physical therapists and VDT operators.

For physical therapists, statistically significant positive associations have been demonstrated for shortwave diathermy and congenital malformations (Taskinen, Kyyronen, and Hemminki 1990), congenital malformations

and perinatal death (Kallen, Malmquist, and Moritz 1982), and the sex ratio of the offspring (Larsen, Olsen, and Svane 1991). No significant differences were observed for spontaneous abortion, heart malformations, stillbirth, birth weight, and prematurity. Significant differences were observed for microwave diathermy and early fetal loss but not for shortwave diathermy (Stewart and Ouellet-Hellstrom 1991; Ouellet-Hellstrom and Stewart 1993).

Increased adverse effects have not been consistently observed, and no specific pattern of effects has been established. Although congenital malformations were elevated in two studies, one of these evaluated congenital malformations and perinatal death (Kallen, Malmquist, and Moritz 1982), while the other examined just congenital malformations (Taskinen, Kyyronen, and Hemminki 1990). Furthermore, the finding of increased congenital malformations and perinatal death was marginally significant (Kallen, Malmquist, and Moritz 1982). Elevated risk ratios were not observed for congenital malformations in other studies (Larsen 1991; McDonald et al. 1987; Ahlborg et al. 1989), although the study by Larsen is the most appropriate for comparison. In regard to perinatal death, no study has found an increased risk of just this end point. The increase in gender-specific risk is unique to that study (Larsen, Olsen, and Svane 1991) and should be considered as hypothesis generating. No difference in sex ratio was observed in a Swedish study (Kallen, Malmquist, and Moritz 1982). The modest increase in early fetal loss with use of microwave diathermy in one study (Stewart and Ouellet-Hellstrom 1991) was not observed in studies that examined spontaneous abortion and microwave diathermy (Taskinen, Kyyronen, and Hemminki 1990; Larsen, Olsen, and Svane 1991).

In at least four of the studies, temporality was established (Kallen, Malmquist, and Moritz 1982; Taskinen, Kyyronen, and Hemminki 1990; Larsen 1991; Larsen, Olsen, and Svane 1991). A dose-response effect has been observed. Taskinen reported a dose-related increase in spontaneous abortions in pregnancies greater than 10 weeks. A reversal of ef-

fects was determined for congenital malformations by weekly exposure to shortwave diathermy. An OR = 2.7 was observed for work between 1 and 4 hours, but the OR decreased to the null value for shortwave diathermy  $\geq 5$  h/wk (Taskinen, Kyyronen, and Hemminki 1990). Larsen found increasing odds ratios for gender distribution of the offspring by both a time-weighted exposure index and the time spent per week in a short-wave room. These results were highly significant ( $P < 0.001$ ) in a test for trend (Larsen, Olsen, and Svane 1991). A dose effect was also found in the data of Kallen when odds ratios are estimated for the "seldom" (OR = 0.40) and "often + daily" (OR = 2.03) categories of shortwave use (Kallen, Malmquist, and Moritz 1982). No significant dose-related effects were found in a study of congenital malformations (Larsen 1991). The OR for early fetal loss increased with increased use of microwave diathermy (Stewart and Ouellet-Hellstrom 1991).

In studies of VDT operators, there is the potential for recall bias in retrospective case-control designs. Recall bias occurs when one group does not accurately report exposure information, thereby leading to exposure misclassification. For example, if the cases overreport exposure, it can have the effect of increasing the reported risk estimates. In one study, the authors suggest that because the administration of their questionnaire was 2.5 years after the first trimester, recall bias may have been possible (Goldhaber, Polen, and Hiatt 1988). Ericson and Kallen (1986b) report finding indications of recall bias.

Other researchers compared exposure information provided by cases and controls with information provided by employers. Nielsen and Brandt (1990) conclude that it is unlikely that recall bias could explain the absence of association found in their study. McDonald et al. (1988c) conclude their findings could be due to recall bias, because "Interviews were conducted at a time when there was widespread public concern on the question [of VDT use and pregnancy outcome] and there was thus the possibility that both interviewer and subject might be influenced

by the outcome of pregnancy when describing and recording the use of VDUs." They report finding evidence of recall bias in a follow-up study. Bryant and Love (1989) designed a study to include pre- and postnatal control groups, based upon the premise that prenatal controls "may be less likely to dismiss minor exposures as insignificant," since they do not know the outcome of their pregnancies yet. They found that postnatal controls may have underreported VDT exposure: "cases reported more exposure to very small amounts of VDT exposure than the postnatal controls, but that this discrepancy does not occur when only prenatal controls are used." In this case, underreporting of VDT exposure would have increased the odds ratios for the cases versus postnatal controls, providing an overestimation of risk.

The strength of the observed association of the point estimates in most studies was "none" (rate ratio = 1.0 to 1.2) to "weak" (rate ratio = 1.2 to 1.5), using the scale suggested by Monson (1990). Both positive and negative associations for the same end point have been reported. Generally, the point estimates of risk are near the null value, and the confidence intervals, although relatively narrow, include the null value. This indicates that, generally, the magnitude of the risk estimates is small, and the estimates are not significantly different from the null value. Hence, the likelihood of these being chance occurrences is increased. In some cases the confidence interval is broad, indicating small sample size and that the precision of the estimate is low. Such is the case in the observed increase in hydrocephalus reported by Brandt and Nielsen (1990).

According to Sir Austin Bradford Hill (1965), "Whether chance is the explanation or whether a true hazard has been revealed may sometimes be answered only by a repetition of the circumstances and the observations." In the studies reviewed above, no strong, consistent association has been observed, i.e., repeatedly observed. Two studies found a statistically significant positive association between VDT use and spontaneous abortion (Goldhaber, Polen, and Hiatt 1988;

McDonald et al. 1988c), although both groups of researchers felt that recall bias could possibly explain the results. Other studies have found both negative and positive associations between VDT use and spontaneous abortion. The only study actually to include RF measurement data did not show an increased risk of spontaneous abortion (Schnorr et al. 1991). In regard to congenital malformations, the data of Ericson and Kallen (1986b) suggested about twice the risk of birth defects for VDT use versus no use. Other researchers have not observed the same association. Kurppa et al. (1985) and Brandt and Nielsen (1990) found adjusted odds ratios of, respectively, 0.9 (95% CI = 0.6 to 1.2) and 0.95 (95% CI = 0.76 to 1.20). McDonald et al. (1988c) determined the relative risk for any defects to be 0.94 (90% CI = 0.78 to 1.13).

The observed associations have not displayed specificity. The types of outcomes evaluated are not limited to VDT users but appear in the general population. In studies of congenital malformations, no specific pattern of malformation type has been established. The data of Ericson and Kallen (1986b) were not specific in regard to type of malformation, and the results were interpreted very cautiously by the authors. Kurppa and coworkers (1985) found a nonsignificant increase in cardiovascular effects, while McDonald et al. (1988c) found a significant increase in urinary defects. Brandt and Nielsen (1990) found a significant, but imprecise, increase in hydrocephalus, but no significant increases in malformations of the heart, blood vessels, or urinary system.

The data are inconclusive concerning the existence of a dose-response effect. Ericson and Kallen (1986b) demonstrated "a tendency for a dose-related effect" for spontaneous abortion or birth defects, but this could be attributed to recall bias. McDonald et al. (1988c) found a statistically significant dose-response trend for current pregnancies but not for previous pregnancies. Goldhaber, Polen, and Hiatt (1988) found a dose-response effect for the administrative support/clerical occupational group but not for three other occupational groups or for all

groups combined. In a discussion of Goldhaber's results, Windham et al. (1990) conclude, "The fact that this pattern of excess risk was not consistent across occupational categories suggests that other factors may be involved including stress or ergonomic factors, inclusion of hours when the VDT was not actually in use, chance, or small numbers." NIOSH workers observed no dose-response relationship for time of use and spontaneous abortion (Schnorr et al. 1991). Brandt and Nielsen (1990), Nielsen and Brandt (1990), and Windham et al. (1990) found no association between time of use and adverse reproductive outcome. In discussion of a possible dose-response relationship, Bryant and Love (1989) state, "While the crude odds ratios did increase across strata with increasing exposure levels when the prenatal control group was used, none of the crude odds ratios were significantly different than one, nor did tests for heterogeneity of odds ratios show the odds ratios to be different from one another. No such trend was found with postnatal controls."

Another criterion useful in interpretation deals with the biologic plausibility of an effect. This criterion must be interpreted with some circumspection, because, as Hill (1965) stated, "What is biologically plausible depends upon the biological knowledge of the day." With the present state of understanding of mechanisms of interaction and biologically effective levels of nonionizing radiations, adverse reproductive outcomes do not seem biologically plausible, unless the levels of RF radiation at the VDT operator position were substantially higher than those reported to date. The study by Schnorr et al. (1991) lends support to this vein of thought. The detailed measurements of VDT fields (Fell 1990) used in the exposure assessment have been reviewed earlier. The measured levels were well below current exposure guidelines; therefore, no adverse effects would be expected, as was the finding in that study. Consideration of hygienic measurements led Kurppa and colleagues to conclude that "the allegation that VDT exposure would result in birth defects had a low prior probability. The a posteriori credibility for such a causal association was not increased by

our results" (Kurppa et al. 1985). Polifka and Friedman (1991) assert that "radiation emissions from VDUs are very low, often being less than background levels and invariably of a magnitude that is very unlikely to have any biologic effect."

Some of the reported associations could possibly be explained by other factors, such as stress and ergonomics. It has been shown that stressing of pregnant test animals by immobilization may affect fetal development (Chernoff et al. 1987). A number of studies have found that using VDTs may increase job stress and that stress indicators are measurable (Gardner, Ruth, and Render 1988; Smith et al. 1981; Gao, Lu, and She 1990; Schreinicke et al. 1990). Chernoff, Rogers, and Kavlock (1989) have reviewed published studies on the effects of stress in humans and animals on reproduction. In regard to the length of use of VDTs each week, Rigau-Perez (1990) commented, "That ostensibly deleterious effects of VDT use could in fact be due to physical or psychological stress is bolstered by epidemiologic studies that point to greatest risk in the women who use VDTs for more than half of their work week."

As noted earlier, only one of the studies reviewed, that by NIOSH researchers (Schnorr et al. 1991), included field measurements as part of the exposure assessment. Other studies evaluated potential associations between reproductive outcome and VDT use by utilizing questionnaires and occupational titles. Although independent corroboration of the results is necessary, the strength of the design used by NIOSH and the absence of adequate evidence to the contrary in other epidemiology studies greatly enhances the position that human exposure to VLF fields associated with VDTs is not associated with adverse reproductive outcomes. Other reviews of the strengths and limitations of these epidemiology studies have been published (Bergqvist 1984; Marriott and Stuchly 1986; Kavet and Tell 1991; Marcus 1989, 1990; Mackay 1987; WHO 1987; ILO 1994).

Individually, none of the criteria used in the critique earlier invalidate the hypothesis of causation of RF-induced birth defects in ex-

posed human populations. However, viewed collectively, they provide a mechanism by which we can critically evaluate cause-effect. The existing data lend support to the conclusion that a causal link does not exist between work as a (female) physical therapist and spontaneous abortion, heart malformations, stillbirth, birth weight, and prematurity. No conclusions can be reached for physical therapists in regard to congenital malformations and gender distribution. Obviously, both of these end points require further evaluation before sufficient data are available to allow reliable conclusions. In regard to VDT operators, the weight of the available epidemiologic information supports the conclusion that exposure to RF radiation and fields associated VDTs does not cause adverse reproductive outcomes. A similar conclusion was found by the International Labour Organization (ILO 1994). However, the main pillar supporting this conclusion is the single study by NIOSH. It is necessary that this study be replicated by an independent research team using a similar design.

### 3.5.6 Cancer

Cancer, as an end point, has received relatively little study. The few published studies have addressed estimates for workers and the general public.

#### 3.5.6.1 Workers

Cancer mortality was examined in the cohort study of naval personnel who worked around radar (see Section 3.5.2). There was a nonsignificant increase (mortality ratio,  $MR = 1.40$ ) in the FT + AT group for malignant neoplasms of the lymphatic and hematopoietic system, while the entire high-exposure group had an  $MR = 1.18$ . When analyzed by Hazard Number, those subjects who were grouped in the highest category of potential hazard had elevated MRs for malignant neoplasms of the lymphatic and hematopoietic system and the respiratory tract, although only the last disease was significantly increased ( $P < 0.05$ ). An ex-

amination of the specific cause of death from malignant neoplasms of the lymphatic and hematopoietic systems showed seven types of neoplasia. This included four types of leukemia, with myeloid occurring most frequently (Robinette, Silverman, and Jablon 1980). No data on smoking history were available (Silverman 1985).

Overall cancer mortality in Moscow embassy personnel was less than controls, with a  $SMR = 0.89$  (95%  $CI = 0.5$  to  $1.4$ ). There were elevated SMRs for leukemia, breast cancer, and cervical cancer. None of these were statistically significant, but the number of observations was small. Also there were no significant findings in cancer morbidity (Lilienfeld et al. 1978).

The cancer mortality experience of members of the Rad Lab staff was also generally low. Cancers accounted for about 25% of the deaths. Over 80% of the 99 neoplasms were from four major sites: digestive organs and peritoneum (25%), respiratory system (23%), genitourinary organs (20%), and lymphatic and hematopoietic tissue (13%). SMR point estimates for five types of cancer were nonsignificantly increased: skin, prostate, testis and other genital organs, Hodgkin's disease, and benign neoplasms. SMRs were significantly lower than expected for U.S. white males for the following cancers: all malignant neoplasms, digestive organs and peritoneum, stomach, large intestine, respiratory system, and lung. When compared with a second control group, physician specialists, death due to malignant neoplasms of the gall bladder and bile ducts showed a marginally significant increase ( $RR = 4.08$ ,  $P = 0.0435$ ). Risk ratios for leukemia and brain cancer were less than unity. SMRs were determined for high-, medium-, and low-exposure groups, with the finding of no statistically significant increases in mortality for any type of cancer (Hill 1988).

Another study of U.S. Navy personnel looked at the incidence of first hospitalization for leukemia among active (1974 to 1984) naval personnel (white men). When analyzed by occupation, only 1 of 95 navy occupations, electrician's mate, had a marginally significant increase in the standardized incidence ratio.

However, this occupational group is not known to be exposed to RF fields but to power-frequency fields (ELF). The authors suggest that the finding of no increased risk of leukemia in occupations exposed to electromagnetic radiation other than at 60 Hz "may be because of the lack of statistical power to detect a difference or may represent a genuinely low risk of developing leukemia during active-duty service in occupations other than electrician's mate" (Garland et al. 1990).

Hamburger, Logue, and Silverman (1983) report finding eight malignancies and three nonmalignant neoplasms in male physical therapists. Three of these were malignant melanomas, which they conclude is "greater than might be expected for white males in the 35-39 age group." The neoplasms could not be associated with a specific type of diathermy.

A number of descriptive studies have been published since 1979 that address cancer mortality and work in occupational classifications that have potential exposure to electric and magnetic fields. Typically, the occupational classifications are quite broad and provide no specific information on potential exposure to any agent. Some of the classifications appear to have the potential for exposure to RF fields, some have the potential for exposure to ELF fields, while others have the potential for exposure to both. These studies lack information concerning exposure doses and spectral distribution of the exposure field. However, we will review these studies since they may provide information that is suggestive of areas needing further research.

Milham (1982) determined proportionate mortality ratios (PMR) for death by leukemia and acute leukemia for white males in Washington State and published the results as a letter to the editor of a medical journal. Four of 11 occupational classes (radio and telegraph operators, television and radio repairmen, electrical engineers, and [arc] welders) have the potential for exposure to RF electromagnetic energies. Acute leukemia was significantly different from the U.S. population for acute leukemia ( $PMR = 291$ ,  $P < 0.01$ ) for TV and radio repairmen. These findings should be viewed as hypothesis generating, since the

study does not appear to be designed a priori to study leukemia mortality in men exposed to electric and magnetic fields. Sheikh (1986) observed that this study calculated 34,444 PMRs (158 causes of death  $\times$  218 occupational classes). At the 5% level, one would expect 1700 PMRs to exceed the null value. Sheikh notes, "For each cause of death in this study, PMRs in three occupational groups were significantly greater than 100%, a number of PMRs expected to be greater than 100% by chance. Consequently the apparent associations between certain electrical occupations and leukemia could be chance occurrences."

In a later study, Milham (1985a) calculated PMRs for white males in the state of Washington using death records (1950 to 1982). Workers in 9 of 219 occupational classes were believed to have "intuitive exposures to electromagnetic fields." By occupational class, where there is the potential for RF exposure, only TV and radio repairmen had significantly elevated ratios (PMR = 344). This was for acute leukemia.

Davis and Mostofi (1993) reported a statistically significant excess of testicular cancer in policemen in two counties in Washington State (O/E = 6.9,  $P < 0.001$ ). According to the authors, these policemen had a practice in common of resting a radar gun in their lap while the gun was on. This hypothesis requires further study with a more rigorous design including a better defined exposed population, matched controls, confounder control, and exposure estimates including microwave levels and exposure duration.

Savitz and Calle (1987) performed a meta analysis of 11 studies that had examined the association between leukemia and occupational exposure to electric and magnetic fields. Most of those studies had used measures of disease frequency that did not allow the determination of disease rates. Savitz and Calle compiled information by occupation and calculated relative risks. For occupational classification with potential RF exposure, there were statistically significant associations for telegraph, radio, and radar operators for total leukemias (RR = 1.8, 95% CI = 1.4 to 2.6),

acute leukemias (RR = 2.1, 95% CI = 1.3 to 3.3), and acute myelogenous leukemias (RR = 2.6, 95% CI = 1.4 to 4.4).

### 3.5.6.2 General Population

Milham (1985b) examined cancer deaths among amateur radio operators. Information on the cause of death was obtained for males from California (CA) and Washington (WA) who had been members of the American Radio Relay League (ARRL). PMRs were calculated using U.S. age-specific, white male death frequencies. Statistically increased causes of death were found for all leukemias (PMR = 191,  $P < 0.01$ ), myeloid leukemia (PMR = 281,  $P < 0.01$ ), acute myeloid leukemia (PMR = 289,  $P < 0.01$ ), and chronic myeloid leukemia (PMR = 267,  $P < 0.05$ ). From examination of the listing in the ARRL magazine of occupation at death, Milham concluded that work in occupations involving potential exposure to electromagnetic fields probably does not explain the observed excess. From Milham's data, Savitz and Calle (1987) estimated a risk ratio = 1.9 (95% CI = 1.2 to 2.8) for total leukemia. These results were not peer-reviewed but published as a letter in a journal.

Milham extended this study and calculated SMRs for radio amateurs; 67,829 amateurs were identified from records of the Federal Communications Commission (FCC) and evaluated for cause of death. In this group there had been 2083 deaths in CA and 402 in WA. SMRs (as a percentage), determined using expected deaths for the general population, were significantly lower for death by all causes, malignant neoplasms, circulatory diseases, respiratory diseases, and accidents. Significantly increased SMRs were found for other lymphatic tissue deaths in CA (SMR = 170) and CA + WA (SMR = 162, 95% CI = 117 to 218), but not for WA (SMR = 115). Lymphatic and hematopoietic tissue malignancies were significantly elevated only for CA deaths (SMR = 129). Death by prostate cancer was significantly elevated in WA (SMR = 195). Death by leukemia was nonsignificantly increased. In an analysis of cause of

death by type of leukemia, there was a significant increase for acute myeloid leukemia (SMR = 176, 95% CI = 103 to 285) but not for other leukemia types. Milham states that the SMRs are underestimated because female amateurs were eliminated from the mortality group but not from the total population. Also, death rates in CA and WA are lower than the U.S. rates used in calculations. From occupational information on death certificates, he estimated that around 31% of the amateurs from WA had jobs that would have exposed them to electromagnetic fields at work. Comparable information from the CA group was not available (Milham 1988a).

It has been suggested that the increase observed in lymphatic and hematopoietic cancers may be due to AIDS-related cancers in San Francisco, because most deaths in this study were in CA. Also, the increase in lymphomas is not unique to radio amateurs, but is a general phenomenon in the United States (Kurt 1988). Milham (1988b) contends that this is not supported because death rates for lymphomas in CA and WA are lower than in the United States, and there is no trend of increasing mortality in the youngest license class.

In another letter, Milham (1988c) reported SMRs by FCC license class for radio amateurs. Because there is a general trend of increasing age by more advanced class, class may "be a crude measure of duration of licensing." Technicians had significantly elevated ratios (SMR = 163) for lymphatic and hematopoietic cancers, while those with a general license had increased multiple myeloma and other lymphomas (SMR = 184). A number of other SMRs were elevated but none significantly. No general trend was observable in the data for death by all causes, all malignant neoplasms, brain cancer, lymphatic and hematopoietic cancer, all leukemias, and myeloid leukemia. Milham notes, "All license classes with the exception of the novice class show modest increases in mortality in the myeloma/other lymphoma rubric. This may indicate that members of the novice class have not been exposed long enough to fulfill a cancer latency period or that novices may

have less exposure to whatever carcinogenic agents may be operating."

Lester and Moore published two studies dealing with cancer mortality and living near air force bases and airports. One study was based on the hypothesis that line-of-sight radar transmission may be associated with cancer patterns in a community. They identified first-diagnosis cancer cases in Wichita, Kansas, for the years 1975 to 1977. The addresses of subjects in census tracts were ascertained and terrain maps used to determine the midpoint elevation. They postulated that individuals living on the crest of a hill would have a higher incidence of cancer than those individuals living in the same line of sight but in a valley. However, their results showed no correlation between living at higher elevation and cancer incidence. By assuming that the terrain provided a shielding effect, which they treated as a confounder, terrain maps were used to determine the degree of shielding with a finding that 30 census tracts were unshielded, 32 had one shield, and 14 tracts had two shields. After adjusting their data for shielding, they found that cancer morbidity, but not mortality, was significantly ( $P = 0.034$ , one-tailed test) correlated with shielding, i.e., the incidence was highest in the unshielded tracts and lowest in the tracts with two shields. An analysis by cancer type showed significance for malignant neoplasms of the bone, connective tissue, skin, and breast, with breast cancer occurring most frequently (Lester and Moore 1982a). This study did not include community controls and exposure information. Apparently it was not determined how long study subjects lived in Wichita or resided at the locations used in the study. Hence, it is not possible to ascertain if the disease preceded perceived exposure. No information is provided on demographics, familial history of cancer, personal habits, or potential occupational exposures.

Lester and Moore (1982b) ascertained cancer mortality data for individuals living in 92 "case" counties having U.S. Air Force bases. An identical number of control counties, which had no air force base, were selected from the same state as the case county. The control counties were similar in population

but not necessarily in geographic and demographic factors. Age-adjusted cancer mortality was determined by sex from cancer maps for each county for 1950 to 1969. A numeric coding scheme was used to indicate whether the county information was significant.

Statistical analysis was performed for correlated proportions of counties with air force bases versus those not having bases. Marginally significant differences in cancer mortality were reported for men ( $P = 0.04$ ) and women ( $P = 0.02$ ).

Polson and Merritt (1985) reanalyzed the data of Lester and Moore. They reassigned 13 bases to different counties because they had been located incorrectly by county, and they reduced the number of counties with air force bases to 91, because one county with 2 bases had been counted twice. They disagreed with control county selection in 43 cases and sex categories in 22 cases (16 counties). They reported nonsignificant findings by sex. In a response to this critique, Lester (1985) corrected his data and analyzed it again, finding that counties with bases still had a significantly different cancer mortality than counties without bases.

Obviously, no reliable conclusions can be made concerning a possible correlation with radar exposure from the studies by Lester and Moore. Based upon their study design, a correlation can only be shown with air force bases and not any specific environmental agent. Even the correlation with bases has been disputed and shown to be dependent upon selection of control county and assignment of sex category.

### 3.5.6.3 Summary and Conclusions

Analysis of morbidity and mortality of naval personnel and Moscow embassy employees found no significant differences for cancer. Rates for Rad Lab employees were not significantly different when compared with the general population, but significant increases were observed in deaths from cancer of the gall bladder and bile ducts compared with physician specialists. Hamburger reported more malignant melanoma than expected, and

Milham observed increased acute leukemia for TV repairmen. The types of significantly elevated cancer were not observed consistently. There are no measurements of exposure in any of these studies, and exposure is inferred.

The studies by Milham and others (dealing with potential occupational exposures) have been used in developing a hypothesis that exposure to electromagnetic fields may be associated with cancer. However, the studies have not controlled for other potential exposures for ham radio operators, including electric shock, exposure to airborne contaminants from soldering and degreasing, and potential ingestion of lead and other metals from workbench contamination during soldering. Another complicating factor, as discussed earlier for occupational cancers, is that it is not clear what electromagnetic exposure these hobbyists received by either dose or spectral distribution.

Although some studies do indeed demonstrate associations between inferred exposure to RF electromagnetic fields and cancer, there are no consistent findings among the various researchers. The finding reported most consistently is an association with leukemia, although this observation was only significant in the work by Milham. The reported strength of association is moderate in the work by Milham, while there is no to weak association in other studies. There is no dose-response effect. For the most part, the results are not statistically significant, and increased point estimates may be due to chance. The hypothesis that RF-field exposure may be associated with cancer, especially leukemia, would be strengthened if there were a strong animal model, but adequate studies have yet to be published.

In conclusion, the data do not support the finding that exposure to RF fields is a causal agent for any type of cancer. For the most part, this conclusion has been reached not because of the strengths of the reviewed studies but because of the limitations of these studies. Obviously, it would be preferable to reach such a conclusion after having reviewed replicates of well-designed studies that consistently report no association, instead of after

reviewing studies with many limitations, some of which report moderate elevations in point measures of risk. Although this may be acceptable to the scientist, it is usually unacceptable to members of the general public where there is a strong measure of suspicion that RF and ELF fields may cause cancer, largely fueled by reports in the popular press. To help answer these concerns, health professionals and public officials need quality information from both laboratory studies and epidemiologic studies. Presently, such information is lacking. Only when studies adequate to withstand not only the rigor of scientific review, but also scrutiny by public interest groups and political interests have been published, can these questions be answered.

### 3.5.7 Skin

Occupational dermatoses have been reported, primarily on facial skin of VDT operators. Principally, theories dealing with emissions from VDTs have involved the static electric field, but some researchers have designed studies that examined ELF and RF fields (Swanbeck and Bleeker 1989; Sandstrom, Stenberg, and Mild 1989; Bergqvist and Wahlberg 1994).

Swanbeck and Bleeker (1989) evaluated 30 patients who had experienced skin problems when working with VDTs. They were challenged with two similar VDTs, one having relatively strong electrostatic and electromagnetic fields while the other had much weaker fields. Humidity was controlled at 25% and 60% in two trials. About 80% of the patients developed some type of skin problem while using either VDT for 3 hours in an environment with 25% relative humidity. One to two weeks later, 19 of the patients were retested at the same VDT they had used initially, but at 60% relative humidity. Sixty-eight percent (13) experienced skin reactions. Eleven of those 13 patients reacted during a later test at 60% relative humidity where the VDT was switched off and covered with a cloth. The authors conclude "that symptoms appear irrespective of which VDU is used, the one with

strong or the one with very weak electrostatic or electromagnetic fields. The high percentage of subjects reacting when the VDU was turned off also indicates, in our opinion that it is unlikely that the electrostatic and electromagnetic fields in front of VDUs are of major importance with regard to provocation of skin problems."

In a cross-sectional study of 353 office workers, Bergqvist and Wahlberg (1994) reported a nonsignificant increase in risk for skin symptoms and calculated accumulated exposures, but not for current exposures. They found no associations between "erythema or symptoms and average or maximum exposure to these fields during the 5 years preceding the dermatological examination." These researchers conclude that nonspecific erythema seems to be associated with high perceived work pace and limited rest breaks, while skin symptoms (questionnaire data) are correlated with high perceived work load.

### 3.5.8 Accident and Incident Reports

A number of reports of acute health effects attributed to RF overexposure have been made. Effects have been reported to the eyes, skin, nervous system, and reproductive system. The reports involve both members of the public and workers, with radar units and microwave ovens the sources most frequently cited. Most reports provide narrative detail of exposure of a single individual, although one report addresses a line crew.

#### 3.5.8.1 Ocular Effects

The first documented incident report of cataracts was made by Hirsch and Parker (1952) of a 32-year old microwave technician who developed bilateral nuclear cataracts. The subject had been employed in radio repair and was active as an amateur radio operator. He had operated a microwave test bench for about a year and had a habit of placing his hand in front of an operating horn antenna to sense

the heat. This required that he look into the antenna at a very close distance. Just prior to presenting himself for medical examination, "he was engaged for a period of three days during which he worked intermittently, from six to eight hours at a stretch, with the output array quite close (10 to 50 cm.) to his head."

An evaluation of a purported case of microwave-induced cataract in a radar technician found no appreciable exposure to x-radiation or microwaves. The cataract was unilateral and classified as a contusion cataract due to ocular trauma in childhood (Dougherty et al. 1965). Ocular evaluation of a microwave-oven repairman who was exposed at 20 mW/cm<sup>2</sup> (2.45 GHz) showed that the individual had no cataracts but did have refractive error that was "possibly related to physiologic aging-induced presbyopia" (Rose et al. 1969).

Zaret has reported a number of occurrences of cataracts in workers involved with radar (Zaret 1975; Zaret and Snyder 1977), communications (LaRoche, Zaret, and Braun 1970), microwave ovens (Zaret 1974a), CRT displays (Zaret 1980a), and VDTs (Zaret 1980b, 1981, 1984), although his findings have been disputed. In one report, he briefly discussed 42 cases of cataracts in individuals who were presumably exposed to levels in excess of 10 mW/cm<sup>2</sup>. With one exception, work histories were not reviewed, and exposure information was lacking. In the exception, the subject kept detailed records and calculated what he believed his exposure to be during a 5-year period (Zaret, Kaplan, and Kay 1969).

In a later report, bilateral blindness, deafness, and vestibular dysfunction in a 53-year-old repairman were attributed to 27 years of microwave exposure. During the subject's career, he received at least one accidental overexposure when he "was exposed to intense microwave energy at a distance of less than two feet." Zaret (1975) supports the potential for long-term MW exposure by reference to the subject's occupation and by stating that the subject worked prior to establishment of the ANSI standard in 1966. This latter fact was interpreted as meaning that the individual worked in an environment free from controls. However, both the federal government and major industrial users recognized

the 10-mW/cm<sup>2</sup> guideline that ANSI adopted as early as 1953 to 1954. Therefore, dependent upon the employer, it is possible that some level of control did exist during part of the occupational history of the subject. During an ophthalmologic exam, it was noted that both eyes were scarred from prior diathermy therapy and surgery.

LaRoche, Zaret, and Braun (1970) reported four cases of accidental overexposure. In one of these, [unspecified] eye injury was found in 4 of 14 communications' workers purportedly exposed to 790-MHz microwaves from a leaky waveguide. However, only two of the four were known to have actually been present during the incident described. Since preemployment physical data were not available, it is possible that the eye problems preceded the incident. Cataracts were observed in 5 of 17 workers who were potentially exposed when a switch malfunctioned allowing microwave (400 to 450 MHz) leakage from an improperly terminated transmission line. The reported frequency range is beyond that shown to induce cataracts in test animals, especially at the low value of power density reported. The other two cases dealt with two workers in each case, who were purportedly exposed for brief periods at values of power density estimated to be moderately high. In both cases, there were no consistent clinical observations.

Zaret's (1974a, 1974b) contention that bilateral cataracts were caused by emissions from a microwave oven was the basis of a debate in print. His views were challenged by six authorities in the field of RF bioeffects (Michaelson and Osepchuk 1974; Carpenter 1974; Merriam 1974; Donaldson 1974; Appleton 1974b) and supported by one (Bouchat 1974). From the facts presented, it is not possible to conclude that the purported exposure caused the observed lenticular defects.

The case reports of cataract formation in VDT operators are narrative in style and provide insufficient information (Zaret 1980b, 1981, 1984). These reports have been disputed in a critical review by the National Research Council (1983).

Joyner (1989) has examined the outcome of litigation where the claim of microwave-induced cataract by a radar technician was dis-

missed by the Australian Administrative Appeals Tribunal.

Lim et al. (1993) reported an accident that occurred during the inspection of a satellite transmitter. The 3.2-m dish antenna normally operated at 30 W, CW, and 6 GHz, but apparently an illegal transmitter had been attached to the system (Magin 1994). The patient, a 44-year-old man, received two 15-minute accidental exposures. Clinical findings were facial erythema, iritis, a foreign-body sensation in and blurring of his eyes, and abnormal cone function. No baseline examination was available for the patient, so it was not possible to associate the findings with the MW exposure. In terms of potential exposure, the power density for normal operation would be  $\leq 1$  mW/cm<sup>2</sup>. If exposure occurred at the power feed, the subreflector, an open transmitter cabinet, a significantly damaged waveguide, or from a much higher power output (as might have existed with an illegal transmitter) the power density would probably have been much higher. However, this was not addressed in the case report, so one is left to speculate what the power density might have been, although Lim and colleagues note that the "energy emitted by the dish was documented by an investigator from the Federal Communications Commission." FCC investigators did visit the site within 24 to 48 hours after the incident. The purpose of the visit was to investigate an "unlicensed uplink operation," not to determine the emitted energy; no measurements were made (Magin 1994). Reportedly, the inspection positioned the FCC investigators closer to the antenna than the maintenance technician had been, with no adverse effects; however, it is not clear if the illegal transmitter was still in place. According to Magin (1994), there was a claim that the technician's exposure came from a leaky waveguide, but no break was observed in the waveguide during the FCC inspection.

Without actual exposure estimates it is difficult to interpret the results. However, the signs and symptoms reported by Lim et al. (1993) are not unique and occur in members of the general population. These effects have been associated with exposure to other agents, such as UV radiation-induced erythema and

photokeratitis. There is no medical evidence to link positively the reported effects with exposure to MW radiation, although Kues (who is a coauthor in Lim et al. 1993) and colleagues have reported changes in cone function (Kues and Monahan 1992) and the iris (Kues and Monahan 1992; Kues and D'Anna 1987) in test animals exposed at 1.25 and 2.45 GHz.

The penetration depth of 6-GHz MW is relatively shallow. Computer modeling by Hocking Joyner, Fleming, and Anderson (1994) demonstrates that at 5.8 GHz most of the MW power would be deposited within the first millimeter of the skin for two- and three-layer models. If the incident power density were 30 mW/cm<sup>2</sup> (an estimate of worst-case leakage from normal operation), the temperature rise in the facial skin would be around 0.48° C. For the same power density, the maximum temperature rise in the eye would be 0.7° C along the corneal surface. Estimated temperature rise in the retina is modest, between 0.08° C and 0.3° C.

### 3.5.8.2 Nervous System Effects

Williams and Webb (1980) reported an incident involving overexposure of the head and trunk of two flight mechanics to an F-4 aircraft radar operating at > 10 GHz. During maintenance the men were accidentally exposed while located about 8 to 10 feet from the antenna. A postexposure assessment suggested that the power density at 6.5 ft was 379 mW/cm<sup>2</sup>, which the men experienced for 20 minutes. The week after the incident one of the individuals experienced nausea, light-headedness, extreme apprehension, poor appetite, and weight loss. The authors report finding no evidence of neurologic disease and conclude that "the major medical problem was anxiety manifested by loss of appetite."

Forman et al. (1982) described two accidents involving two men on military field maneuvers who were overexposed while facing a portable radar tracking system operating in the x-band (8.2 to 12.4 GHz). The E-field strength was 475 to 580 V/m (~60 to 90 mW/cm<sup>2</sup>). Psychological symptoms in a 54-year-old man included recurrent severe